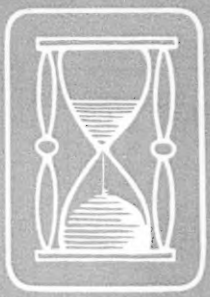
VOLUME 11 • NUMBER 12 • *December 1956*



Geriatrics

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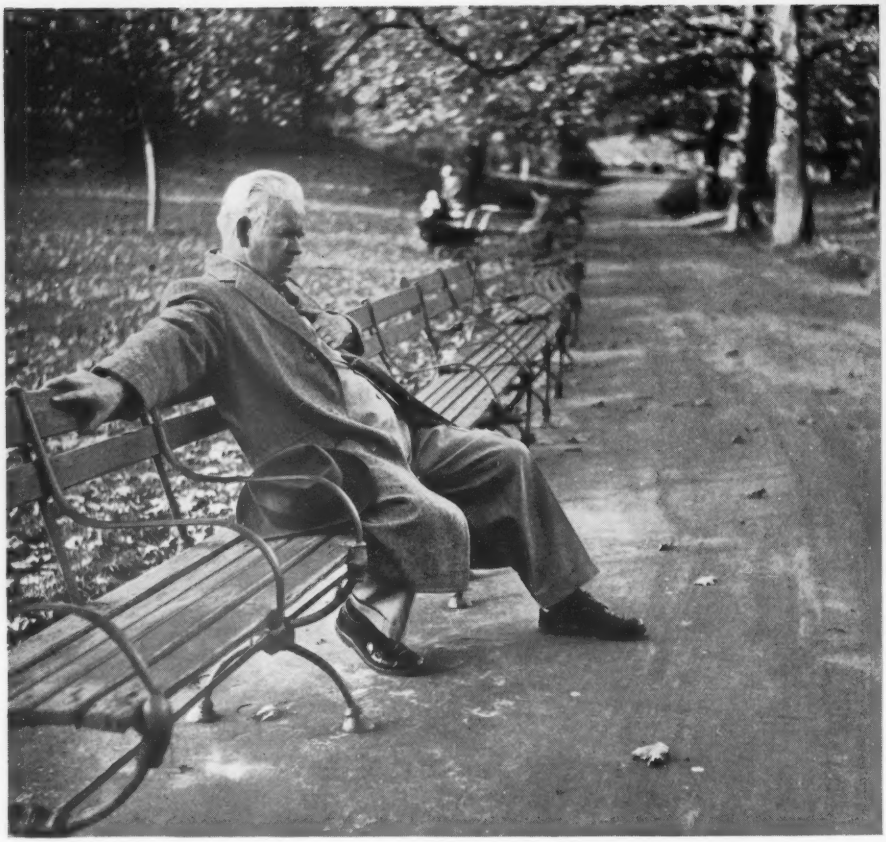

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Dosage: Usually one tablet daily; occasional patients may require two tablets daily, depending on clinical response.

Supplied in bottles of 100 and 500.

*Purified thyroid globulin

References: 1. McGavack, T. H.: Geriatrics *5*:151 (May-June) 1950. 2. Masters, W. H.: Obst. & Gynec. *8*:61 (July) 1956. 3. Kimble, S. T., and Stieglitz, E. J.: Geriatrics *7*:20 (Jan.-Feb.) 1952. 4. Kountz, W. B., and Chieffi, M.: Geriatrics *2*:344 (Nov.-Dec.) 1947. 5. Birnberg, C. H., and Kurzrok, R.: J. Am. Geriatrics Soc. *3*:656 (Sept.) 1955.

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Multiple-dose vials, 10 ml., 25 mg. per ml.

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Geriatrics

Established 1946

Volume 11
Number 12

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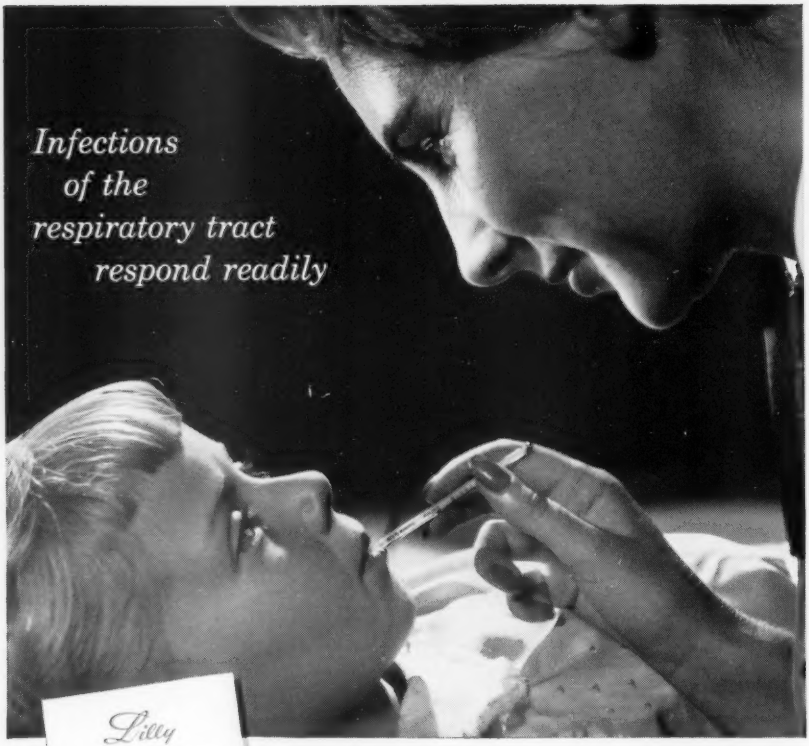

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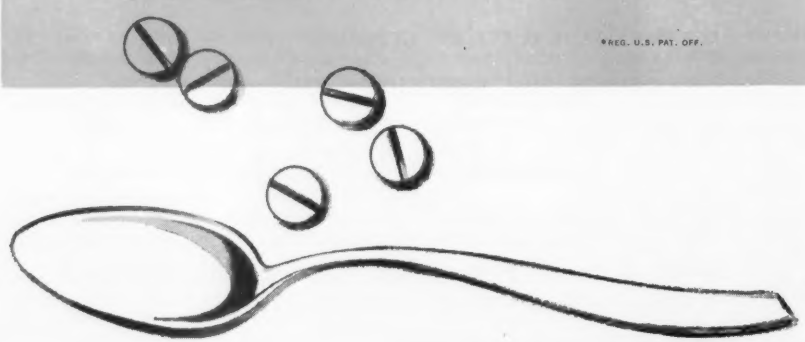

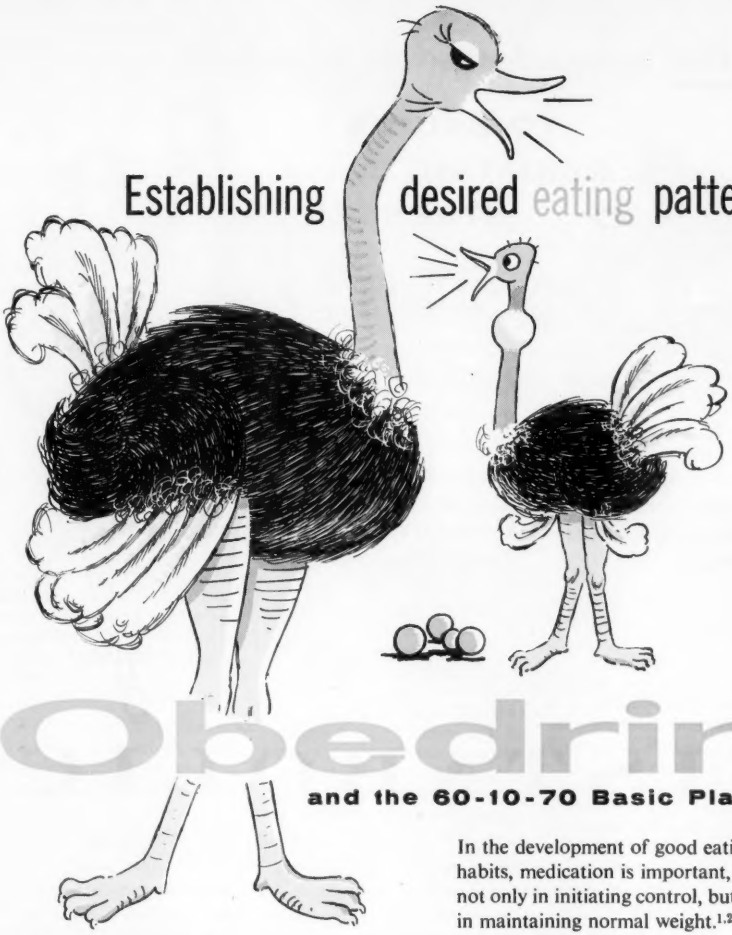

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1. Eisfelder, H.W.: Am. Pract. & Dig. Treat., 5:778 (Oct.) 1954).
2. Sebrell, W.H., Jr.: J.A.M.A., 152:42 (May, 1953).
3. Sherman, R.J.: Medical Times, 82:107 (Feb., 1954).

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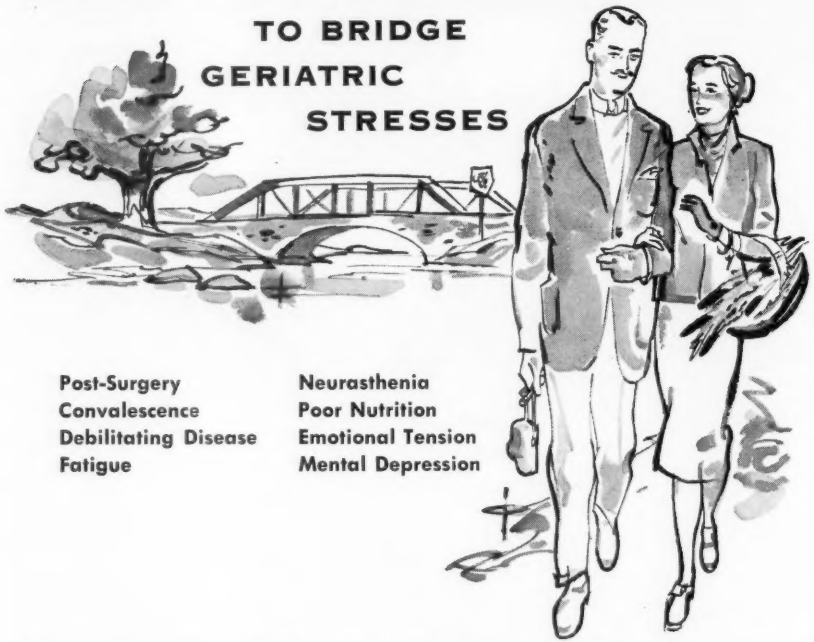
a ***new*** *gerontotherapeutic preparation*



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. . . looking forward

• Although the disabilities of old age generally advance gradually, there may occur some acute episodes threatening life which are thoroughly correctible when their true nature is recognized, says Duane Carr, professor of surgery at the University of Tennessee, writing in the January issue of *Geriatrics*. He discusses various *Intrathoracic Emergencies in the Aged*, such as acute esophageal obstruction from various causes and spontaneous pneumothorax in the elderly person with emphysema. He also reviews the similarity between the clinical picture of acute coronary thrombosis and that presented by some other clinical catastrophes.

• The healthy old person has normal iron stores, and there is minimal exchange between his body iron and the environment, according to Alexander R. Stevens, Department of Medicine, University of Washington School of Medicine, writing on *The Significance of Iron Stores in Later Life*. Iron stores are depleted in iron-deficiency anemia, and increased in other forms of anemia. Iron therapy is never indicated when iron stores are normal or increased. Especially in elderly people, iron deficiency anemia signifies that blood loss has occurred, and the diagnosis carries with it the obligation to find the source of bleeding.

A short symposium, *The Physiologic Aspects of Aging*, is presented from the Conference on Aging held at Galesburg State Research Hospital, Galesburg, Illinois, on May 5, 1956, under the cosponsorship of the Hospital and the University of Illinois College of Medicine. The symposium includes the following authors and papers.

• Nathan W. Shock, director of research, Gerontology Division, National Institute of Health, Bethesda, Maryland, discusses *Age Changes in Some Physiologic Processes*. He points out that: not all physiologic functions change with age; wide individual differences exist in the effects of age; some of the age changes in physiologic functions of the total person can be ascribed to a loss of cellular protoplasm; and there is some evidence that cellular functions change with age. He states that our ultimate goal is to identify the cellular properties that are the basis to the biologic process of aging which is common to all living animals.

• There are changes in the chemical substances of *Brain Composition During the Whole Life Span*, according to Williamina A. Himwich and Harold E. Himwich of the research staff of Galesburg State Research Hospital, Galesburg, Illinois. For example, there is a gradual increase of water at the expense of solid constituents. These changes, with the concomitant morphologic alterations, may represent the basis for mental impairment in the elderly. The paucity of data points to the great need for further research in this field, especially an analysis of human brains at all ages and under a variety of pathologic conditions. They stress that rational treatment must be preceded by a clear understanding of the functional pathology.

• The maintenance of physical fitness with age has become an important national problem because of the increasing proportion of older population, says Ernst Simonson, associate professor, Laboratory of Physiological Hygiene, University of Minnesota. In *Changes of Physical Fitness and Cardiovascular Functions with Age*, he compares the decline of working capacity and performance of people over 40 for various types of work and discusses the physiologic mechanisms involved in the performance drop, the possibility of counteracting aging processes by training, and the relation between heart disease and the aging processes.

For these and other articles, abstracts, reviews, and special features, read every issue of Geriatrics.

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THE CASE FOR EARLY CONTROL OF HYPERTENSION[1]

In the Guest Editorial for GP in July,
Dr. Edward D. Freis reexamines two major questions:

1. Should Hypertension Be Treated Early?

Freis finds the case for early treatment to rest on cause-and-effect evidence: ". . . high pressure, . . . *and nothing else but this high pressure,* creates many if not all the organic manifestations that lead to the final disability and eventual death of the patient." The "evidence presents a cogent argument for the treatment of hypertension early before vascular damage has occurred."[1]

2. What Is the Role of the More Potent Agents? ". . . the evidence . . . suggests that the technique [for the effective and safe use of such agents as ANSOLYSEN] should be more widely learned and employed. Furthermore, . . . the patients with early hypertension, especially those without renal damage, are far more easily controlled, with fewer side effects, than the patients with advanced hypertension."[1]

Freis cautions that these views are not presented as dogma; ". . . they have been developed to show the other side of an argument that seems to have many points in its favor."[1]

1. Freis, Edward D.: Guest Editorial. GP *14*:72 (July) 1956.

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Literature available to physicians—write Medical Service Department.

references: (1) Rottino, A.: Journal-Lancet *71*:237, 1951. (2) Susinno, A. M., and Verdon, R. E.: J.A.M.A. *154*:239 (Jan. 16), 1954.

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*Joseph, M.: Am. J. Surg. *87*:905, 1954.

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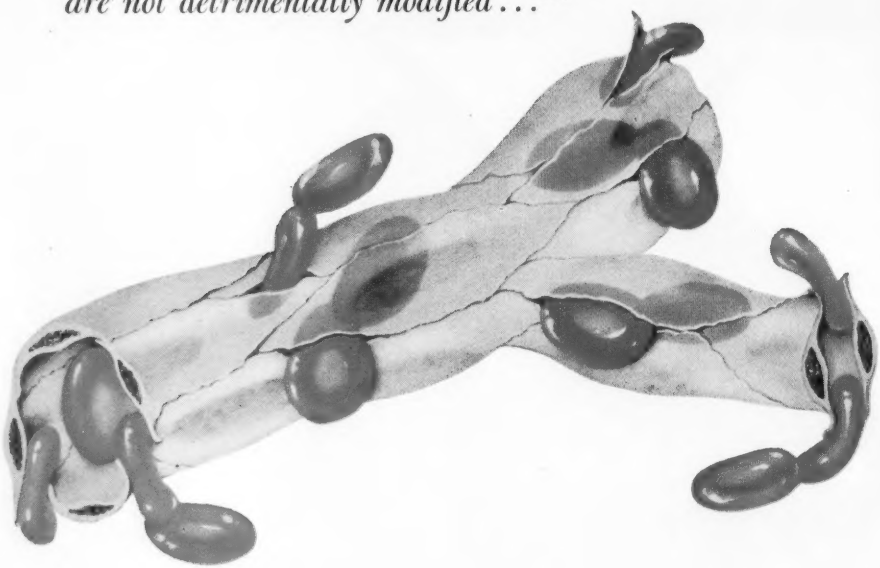

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References: **1.** Martin, G. J., et al.: Exper. Med. & Surg. *12*:535, 1954. **2.** Griffith, J. Q., Jr., and Lindauer, M. A.: Am. Heart J. *28*:758, 1944. **3.** Barishaw, S. B.: Exper. Med. & Surg.: *7*:358, 1949. **4.** Epstein, E. Z., and Greenspan, E. B.: Arch. Int. Med. *68*:1074, 1941. **5.** Warter, P. J., et al.: Delaware M. J. *20*:41, 1948. **6.** Beaser, S. B., et al.: Arch. Int. Med. *73*:18, 1944. **7.** Greenblatt, R. B.: Office Endocrinology, ed. 4. Springfield, Ill., Charles C Thomas, 1952. **8.** Gale, E. T., and Thewles, M. W.: Geriatrics *8*:80, 1953. **9.** Drezner, H. L., et al.: Am. Pract. & Digest. Treat. *6*:912, 1955. **10.** Selsman, G. J. V., and Horoschak, S.: Am. J. Digest Dis. *17*:92, 1950. **11.** Loughlin, W. C.: New York J. Med. *49*:1823, 1949.

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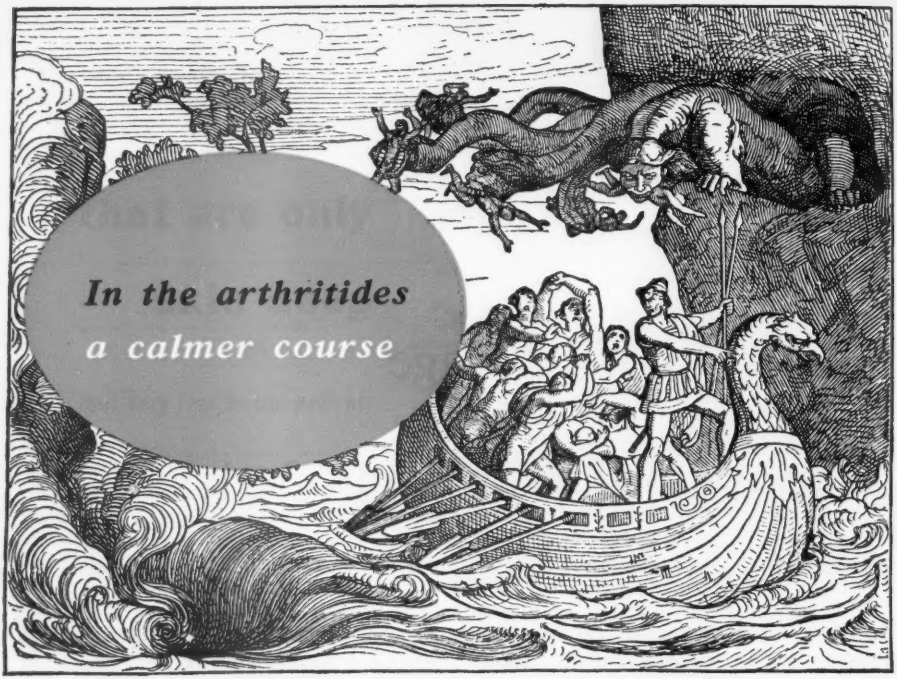

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[1] *Busse, E.A.: Treatment of Rheumatoid Arthritis by a Combination of Cortisone and Salicylates. Clinical Med.* 11:*1105*

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prednisolone and hydroxyzine

Pfizer

combining the newest, safest tranquilizer, ATARAX® + the newest, most effective steroid, STERANE® (prednisolone)

simultaneously controls the symptoms and the apprehension

In Rheumatoid Arthritis, other collagen diseases, bronchial asthma and inflammatory dermatoses

*Trademark

IN DIABETES...

greater security against vascular complications

Increased threat of vascular complications in diabetic patients can result from recurring episodes of inadequate control; at such times amino acids are "wasted" by de-amination in the liver and normal dietary security against lipotropic deficiency fades.

TRADE MARK

Gericaps

(Sherman Lipotropic Capsule) **One capsule t.i.d.**

Gericaps contain the true lipotropics, choline and inositol, which are unaffected by de-amination in the liver. Three capsules daily provide the equivalent of 3 Gm. choline dihydrogen citrate.

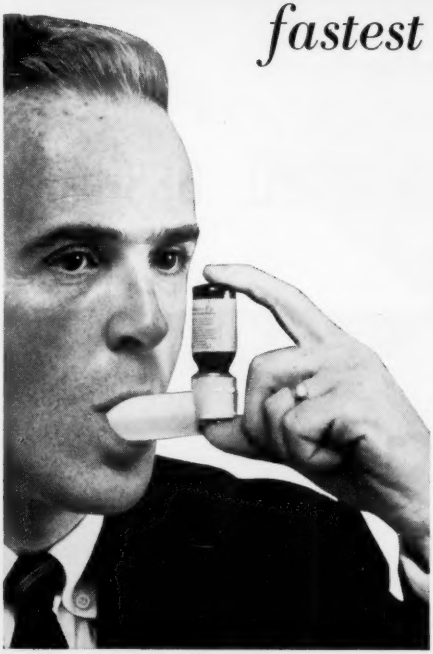
This dose also provides 60 mg. rutin and 37.5 mg. ascorbic acid to maintain or improve capillary integrity, as well as 3000 units vitamin A, 3 mg. thiamine hydrochloride, 3 mg. riboflavin, 12 mg. niacinamide, 0.75 mg. pyridoxine hydrochloride, and 3 mg. calcium pantothenate.

SEND FOR comprehensive review:
"Prevention of Vascular Complications of Diabetes"

SHERMAN LABORATORIES
BIOLOGICALS • PHARMACEUTICALS
WINDSOR • DETROIT 31, MICH. • LOS ANGELES

In Angina Pectoris

Medihaler-Nitro™



fastest relief of the acute attack

MEDIHALER-NITRO is octyl nitrite (1%) in aerosol solution; delivered by metered-dosage nebulization, using the lungs as portal of entry, it assures fastest relief and prolonged effect; it is free from disagreeable, irritating odor, and less apt to produce side actions than are nitroglycerin and amyl nitrite.

To be used only with the MEDIHALER® ORAL ADAPTER made of unbreakable plastic with no moving parts. Medication and Adapter fit into pocket-size plastic carrying case. One or two inhalations provide prompt relief of an attack of angina pectoris.

MEDIHALER...*The New Measured-Dose Principle of Nebulization*

and for definitive therapy... fewer and fewer attacks of less and less intensity

Long-acting tablets containing pentaerythritol tetranitrate (PETN) 10 mg. and Rauwiloid® (alseroxylon) 1 mg. reduce the incidence and intensity of attacks and lead to objective improvement demonstrable by ECG. Dosage: one or two tablets q.i.d., before meals and on retiring

Pentoxylon®

Riker

LOS ANGELES

before

pathetic, atonic, antisocia

after

lert, animated, assured

with

naleptone*

because when depression, mental confusion, emotional lability, irritability, or antisocial attitudes are part of the geriatric syndrome . . . an *analeptic* may be indicated rather than a tranquilizer. The gamut of symptoms caused by hypoxia are effectively relieved or reversed by the cerebral stimulation of ANALEPTONE elixir or tablets.

Formula—*Elixir*, 1 teaspoonful: pentylenetetrazol, 200 mg.; niacin, 100 mg.; Peptenzyme* Elixir q.s.—*Tablets*: pentylenetetrazol, 100 mg.; niacin, 50 mg.; pepsin 1:10,000, 5 mg. Dosage—½ to 1 teaspoonful or 1 to 2 tablets, one to three times per day. Available—in bottles of 8 fl. oz. or 100 tablets.

*T.M.

REED & CARNRICK Jersey City 6, N.J. R&C

For improved protein nutrition

Cerofort®

elixir

(Critically essential L-lysine with essential B vitamins)

Potentiates protein synthesis in:

- *the elderly*
- *the convalescent*
- *the adolescent*
- *the growing child*

Efficient protein synthesis depends upon an adequate intake of proper proportions of all the essential amino acids simultaneously. The biological value of cereal proteins, which comprise 20-40% of total dietary proteins, is limited by a relative deficiency of lysine. Cerofort Elixir supplies physiological amounts of L-lysine to raise the body-building value of many cereals to that of high-quality animal muscle protein. And to aid tissue synthesis, Cerofort Elixir also supplies generous amounts of essential B vitamins.

also available:

Cerofort® tablets

(Critically essential L-lysine with all the important vitamins)

to speed convalescence in major surgery, illness, injury.

White's *first with lysine*

WHITE LABORATORIES, INC.
Kenilworth, N. J.

a new clinical study[1]

adds to the growing promise of

Sparine*

HYDROCHLORIDE

Promazine Hydrochloride

10-(γ-dimethylamino-n-propyl)-phenothiazine hydrochloride

*Trademark

in a diversity

of common clinical conditions

1. Shea, J., et al.: Military Med. 119:221-227 (Oct.) 1956.

Wyeth

Philadelphia 1, Pa.

● SPARINE Hydrochloride provides dramatic control of agitation in the acute psychotic, acute alcoholic, and drug addict. Especially promising has been the minimal toxicity observed—no case of liver damage has been reported.

In a new study, Shea and others[1] find SPARINE effective for control of a wide range of conditions associated with various medical emergencies. In a series of 47 cases the authors found:

"On all but 2 cases the doses used (25 to 200 mg.) permitted satisfactory control of such . . . problems as agitation, anxiety, nausea, vomiting, pain and hiccoughs."[1]

Clinical Report on . . .

PROMAZINE IN THE MANAGEMENT OF MEDICAL DISTURBANCES[1]

Case No.	Age	Diagnosis	Therapeutic Indication	Dose and Route	Duration of Therapy in Days	Response
1	56	Tetanus	Control convulsions and for relaxation	100 mg., q4h, I.V.	2	Good muscle relaxation Opisthotonos—no convulsions
2	36	Duodenal ulcer, D.T.'s	Control D.T.'s and nausea	50 mg., q6h, p.o.	6	No trouble with nausea
3	60	Peptic ulcer and hiatal hernia	For sedation	50 mg., q6h, p.o.	13	Good response—no pains
4	45	Pancreatitis—Gastritis	Hyperactivity	50 mg., q6h, p.o.	7	Good response—pain diminished
	42	Cirrh	Hyper	50 mg., q4h, I.M.	7	G
7	40	Intracranial hemorrhage and M.S.	Pain in muscles	50 mg., q.i.d., p.o.	35	Good control of muscle pain
8	30	Ulcerative colitis	Pain from muscle and vomiting	100 mg., q6h, I.M.	36	Fair response
9	38	Sickle cell crisis Narcotic addict	Control pain	100 mg., q4h, p.o.	3	Good response
10	48	Rt. lower lobe pneumonia Chronic alcoholic	Control activity	100 mg., q6h, p.o.	12	Good response
11	44	Pneumonia	Vomiting and D.T.'s	50 mg., q6h, I.M.	6	Good response, immediate
			Abdominal pain		10	Good pain control
22	13	Uremia	Vomiting	25 mg., q6h	4	Vomiting controlled
23	57	Alcoholic (post)	D.T.'s and pain in chest	50 mg., q.i.d., I.M.	25	Controlled D.T.'s, pain relieved
24	42	Alcoholic (post)	Confused and disoriented	50 mg., q6h, p.o.	27	Fair control
25	71	HCVD—cerebral arteriosclerosis	Behavior problem	50 mg., t.i.d., p.o.	9	Good
26	47	Rheumatoid arthritis Acute excitation	Pain	50 mg., q6h, p.o. 50 mg., q6h, p.o.	3 5	Fair response
	16	Stricture of esophagus Pregnancy—hypertension	Vomiting	50 mg., q6h, I.M. 25 mg., q6h, I.M.	2 3	Controlled vomiting
		Chronic glomerulonephritis	Control nausea and vomiting	50 mg.	9	G

in URINARY DISTRESS

Pyridium®

(Brand of Phenylazo-diamino-pyridine HCl)

provides gratifying relief in a matter of minutes

Painful symptoms impel the patient with acute or chronic pyelonephritis, cystitis, urethritis or prostatitis to seek your aid. In the interval before antibiotics, sulfonamides or other antibacterial measures can become effective, the nontoxic, compatible, analgesic action of PYRIDIUM brings prompt relief from urgency, frequency, dysuria, nocturia or spasm. At the same time, PYRIDIUM imparts an orange-red color to the urine which reassures the patient. Used alone or in combination with antibacterial agents, PYRIDIUM may be readily adjusted to each patient by individualized dosage of the total therapy.

SUPPLIED: In 0.1 Gm. (1½ gr.) tablets in vials of 12 and bottles of 50, 500, and 1,000.

PYRIDIUM is the registered trade-mark of Nepera Chemical Co., Inc., for its brand of phenylazo-diamino-pyridine HCl. Sharp & Dohme, Division of Merck & Co., Inc., sole distributor in the United States.

MERCK SHARP & DOHME
Philadelphia 1, Pa.
Division of MERCK & CO., INC.

*In constipation... "the consistency of the stool is more important than the frequency of defecation or the quantity expelled."**

* Cecil, R. L., and Loeb, R. F., eds.: A Textbook of Medicine, ed. 9, Philadelphia, Saunders, 1955. p. 880.

new

MOLOFAC

Squibb Dioctyl Sodium Sulfosuccinate

relieves or prevents constipation by softening the stools

Molofac softens stools by lowering surface tension in the intestine, permitting water to mix more thoroughly with the fecal matter. Molofac fosters natural, spontaneous defecation... *it is not a laxative or a cathartic.*

In mild constipation—Adults and older children: 1 or 2 capsules daily. Children 6 to 12 years old: 1 capsule daily.

In more severe constipation—Adults and older children: an initial dose of 2 capsules twice daily for three days, with 1 or 2 capsules daily thereafter. Increased dosages may sometimes be required.

NOTE: The stool-softening effect of Molofac is usually evident 1 to 3 days after the beginning of treatment.

Supply: Bottles of 30 and 100 capsules. Each clear, red, one-piece capsule contains 60 mg. of dioctyl sodium sulfosuccinate.

SQUIBB *Squibb Quality—the Priceless Ingredient*

"MOLOFAC" IS A SQUIBB TRADEMARK

30A

"Neither rain, nor snow, nor advancing years shall stay this courier!"

For persons past forty, good health is usually a source of great pride and satisfaction. Each succeeding year seems to heighten their delight and appreciation. To help these "senior citizens" maintain their vigor, prescribe GEVRAL, a comprehensive geriatric diet supplement that provides 14 vitamins, 11 minerals, and Purified Intrinsic Factor Concentrate—all in one convenient, *dry-filled* capsule.

Gevral*

GERIATRIC VITAMIN-MINERAL SUPPLEMENT LEDERLE

Each GEVRAL Capsule contains:

Vitamin A	5000 U.S.P. Units	Rutin	25 mg.
Vitamin D	500 U.S.P. Units	Purified Intrinsic Factor Concentrate	0.5 mg.
Vitamin B_{12}	1 mcgm.	Iron (as $FeSO_4$)	10 mg.
Thiamine Mononitrate (B_1)	5 mg.	Iodine (as KI)	0.5 mg.
Riboflavin (B_2)	5 mg.	Calcium (as $CaHPO_4$)	145 mg.
Niacinamide	15 mg.	Phosphorus (as $CaHPO_4$)	110 mg.
Folic Acid	1 mg.	Boron (as $Na_2B_4O_7.10H_2O$)	0.1 mg.
Pyridoxine HCl (B_6)	0.5 mg.	Copper (as CuO)	1 mg.
Ca Pantothenate	5 mg.	Fluorine (as CaF_2)	0.1 mg.
Choline Dihydrogen Citrate	100 mg.	Manganese (as MnO_2)	1 mg.
Inositol	50 mg.	Magnesium (as MgO)	1 mg.
Ascorbic Acid (C)	50 mg.	Potassium (as K_2SO_4)	5 mg.
Vitamin E (as tocopheryl acetates)	10 I.U.	Zinc (as ZnO)	0.5 mg.

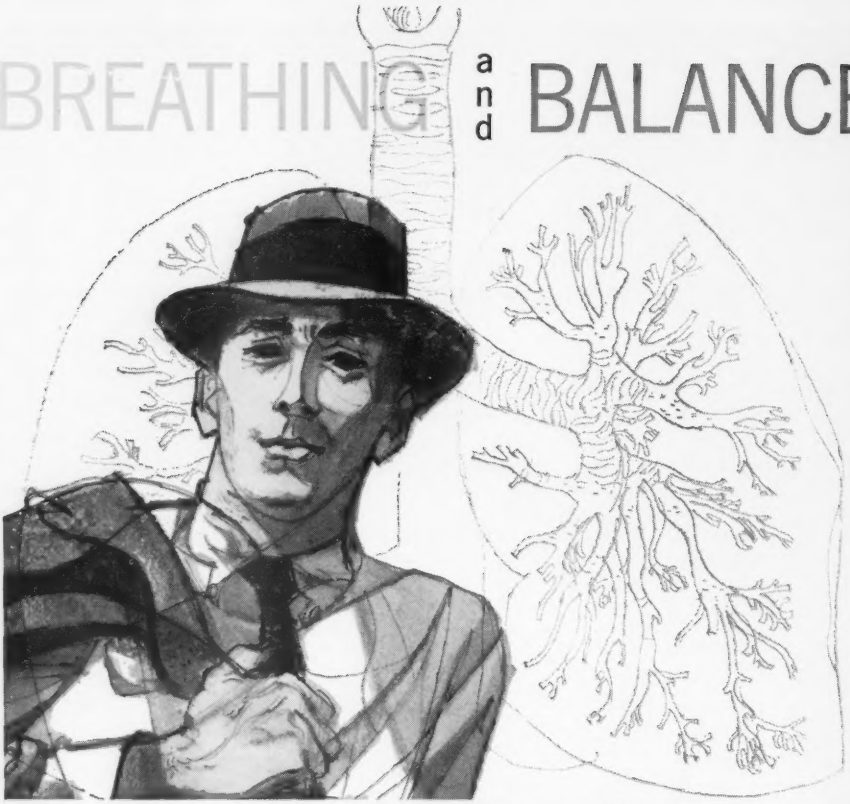
Other Lederle geriatric products include: *GEVRABON** Vitamin-Mineral Supplement Liquid with a wine flavor; *GEVRAL** Protein Vitamin-Mineral-Protein Supplement Powder; and *GEVRINE** Vitamin-Mineral-Hormone Capsules.

for more rapid and complete absorption, freedom from aftertaste. A Lederle exclusive!

Lederle LEDERLE LABORATORIES DIVISION *AMERICAN CYANAMID COMPANY* PEARL RIVER, NEW YORK

*REG. U.S. PAT. OFF.

BREATHING and BALANCE



in bronchial asthma

Sterane®

brand of prednisolone

whenever corticosteroids are indicated

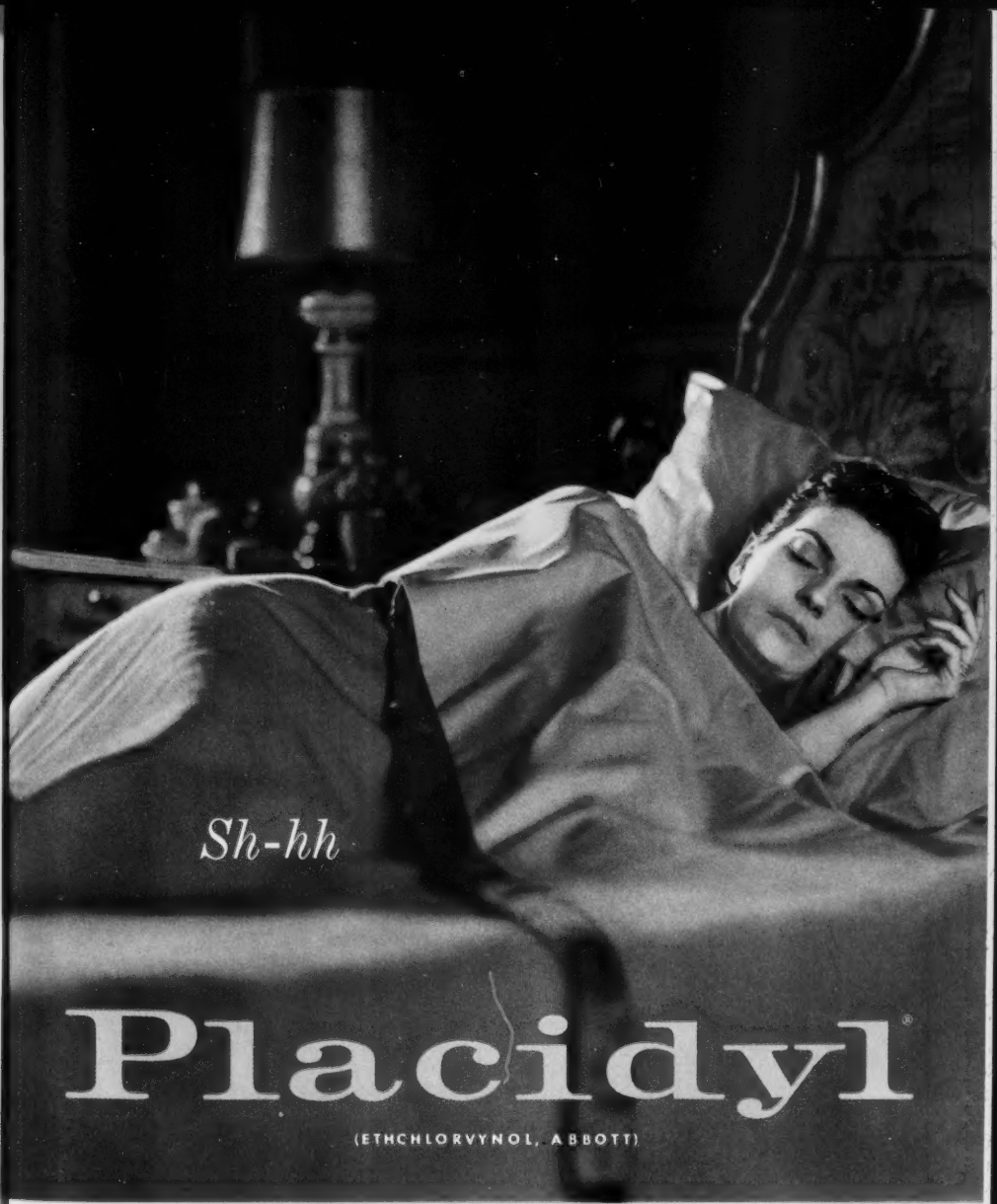
provides restoration of breathing capacity — Relief of symptoms [bronchospasm, cough, wheezing, dyspnea] is maintained for long periods with relatively small doses.*

minimal effect on electrolyte balance — "in therapeutically effective doses . . . there is usually no sodium or fluid retention or potassium loss."* Lack of edema and undesirable weight gain permits more effective therapy particularly for those with cardiac complications.

Supplied: White, 5 mg. oral tablets, bottles of 20 and 100. Pink, 1 mg. oral tablets, bottles of 100. Both are deep-scored.

*Schwartz, E.: New York J. Med. 56:570, 1956.

PFIZER LABORATORIES, Brooklyn 6, New York
Division, Chas. Pfizer & Co., Inc.



nudges your patient to sleep

Nonbarbiturate. Gently calms the nervous insomnia patient, bringing tranquil sleep in 15-30 minutes. Wears off in about 5 hours, so patient normally awakens next day free of hangover. Abbott

611023

prompt

relief

Selsun®

quickest way to relieve the itching, scaling, burning of seborrheic dermatitis and dandruff.

The first few Selsun applications control symptoms —then each application keeps the scalp healthy up to four weeks. Effective in 81-87% of seborrheic dermatitis, 92-95% of dandruff cases. And Selsun is as simple to use as a shampoo. Sold only on prescription, Selsun Suspension comes in 4-fluidounce plastic bottles.

Abbott

611024 ®Selenium Sulfide, Abbott

gentle

is the word

for Noludar

Mild, yet positive in action, Noludar 'Roche' is especially suited for the tense patient who needs to relax and remain clear-headed—or for the insomniac who wants a refreshing night's sleep without hangover. Not a barbiturate, not habit-forming. Tablets, 50 and 200 mg; elixir, 50 mg per teasp.

Noludar® brand of methyprylon (3,3-diethyl-5-methyl-2,4-piperidinedione)

ROCHE

Original Research in Medicine and Chemistry

HOW OLD IS OLD?

"The really old people are those 10 years older than myself."[1]

"In the lay mind, anyone past 60 is ready for the discard . . ."[2]

". . . there are only three principal phases in the span of life: infancy, adolescence and senescence."[3]

"One finds alert, interesting, active folks in the 80's and, on the other hand, there are people in the 20's and 30's who have all the characteristics of old age."[4]

THE REAL QUESTION

To the physician on the firing line of daily practice, the question of "how old is old?" seems academic. To him, a more valid question is "How can I allay the effects of the aging process?"

FIVE PROBLEMS IN AGING

The answer, according to most authorities, is manifold, for five treatable problems seem to predominate. One, obviously, is gonadal hormone decline. Another is mild anemia. A third is the decreased production of gastric and digestive enzymes. Mineral-vitamin deficiency is the fourth. And the fifth – perhaps most important – is inadequate high-quality protein intake.

THERAPY FOR AGING

Judging from this confused clinical picture of aging, therapy for the problem would appear difficult. However, most physicians agree that a product which could correct most or all of these five commonest problems would remove past obstacles to satisfactory response. Such a product would, essentially, be true "preventive geriatrics."

NEOBON'S COMPREHENSIVE FORMULA

NEOBON®, a product of Roerig research, is a blended combination of the five most commonly indicated factors for prevention or treatment of the nonacute conditions of aging. Each soft, soluble capsule provides:

- Non-stimulatory gonadal hormone replacement
- balanced hematinic component
- digestant enzyme replacement
- specially formulated mineral-vitamin combination
- new lysine, for protein improvement*

* Protein deficiency among the aging apparently stems from their excessive intake of white-flour foods which furnish incomplete protein of low biologic value. White bread protein, for example, has been shown by nutrition studies in animals[5] to be deficient only in the amino acid, lysine. In human subjects metabolic determinations indicate that the addition of supplemental lysine to a basal white-flour protein diet can convert a negative nitrogen balance into a positive one.[6]

A WORD ABOUT SYMPTOMATOLOGY

In spite of jokes to the contrary, the patient who states in the professional office that "old age is creeping up" is a rare bird indeed.

Seldom is old age the presenting complaint. Thus the physician, after correcting the specific complaints, must re-evaluate the whole person to judge his candidacy for "preventive geriatrics." Such people have much to gain from NEOBON therapy. The rewards are fuller, more active, more pleasurable years for patients past 40. The daily dose (3 capsules) of NEOBON provides:

L-lysine	150 mg.
Methyltestosterone	3 mg.
Ethinyl Estradiol	0.018 mg.
Pancreatic Substance***	150 mg.
Glutamic Acid	90 mg.
Rutin	15 mg.
Vitamin A (Palmitate)	6,000 U.S.P. Units
Vitamin D (Irradiated Ergosterol)	600 U.S.P. Units
Vitamin E (as Tocopheryl Acetate)	15 I.U.
Calcium Pantothenate	15 mg.
Thiamine Mononitrate (Vitamin B_1)	1.5 mg.
Riboflavin (Vitamin B_2)	1.5 mg.
Pyridoxine Hydrochloride (Vitamin B_6)	1.5 mg.
Niacinamide	150 mg.
Ascorbic Acid (Vitamin C)	150 mg.
Vitamin B_{12} (Oral Concentrate)	3 mcg.
Folic Acid	0.3 mg.
Liver-Stomach Substance**	300 mg.
Iron (from Ferrous Gluconate)	10.2 mg.
Cobalt (from Cobaltous Sulfate)	0.1 mg.
Molybdenum (from Sodium Molybdate)	2 mg.
Copper (from Cupric Sulfate)	1 mg.
Manganese (from Manganous Sulfate)	1 mg.
Magnesium (from Magnesium Sulfate)	6 mg.
Iodine (from Potassium Iodide)	0.15 mg.
Potassium (from Potassium Sulfate)	5 mg.
Zinc (from Zinc Sulfate)	1.2 mg.

**Enzymatically active defatted material obtained from 1,500 mg. whole fresh liver and stomach.

***Enzymatically active defatted material obtained from 750 mg. of whole fresh pancreas.

Dosage: 3 capsules daily, with meals.

Supplied: Bottles of 60 capsules, prescription only.

NEW NEOBON® LIQUID

A GERIATRIC TONIC

Now also available for your consideration is NEOBON LIQUID, which provides hematinic action, improved carbohydrate and protein utilization, gonadal and thyroid hormone supplementation and a mild antidepressant action.

The pleasant tasting liquid is especially indicated when a combined attack against nutritional, physiological and mental depression is indicated. Each teaspoonful (5 cc.) of pleasant-tasting NEOBON LIQUID contains:

Ferrous Gluconate	30 mg.
Ascorbic Acid	50 mg.
d-Amphetamine Sulfate	0.5 mg.
Folic Acid	167 mcg.
Vitamin B_{12}	2.5 mcg.
l-Thyroxine	0.1 mg.
Ethinyl Estradiol	1 mcg.
Methyltestosterone	1 mg.
Liver Fraction I	25 mg.
Ethyl Alcohol	0.5 cc.

Dosage: One teaspoonful twice daily before meals, or as required.

Supplied: In 16 fluid ounce bottles, prescription only.

Bibliography

1. Anonymous. 2. Rosenthal, P.: Geriatrics 10:382 (August) 1955. 3. Lansing, A. I.: Symposium on Problems of Gerontology, National Symposium Series No. 9 (August) 1954. 4. Mason-Hohl, E.: Quoted in W. Va. Med. J. 51:16 (January) 1955. 5. Rosenberg, H. R., et al.: Arch. Biochem. and Biophys. 49:263, 1954. 6. Bricker, M., Mitchell, H. H. and Kinsman, G. M.: J. Nutrition 30:269, 1945. 7. Masters, W. H. and Ballew, J. W.: Geriatrics 10:1, 1 (January) 1955.

ROERIG Rx *CHICAGO 11, ILLINOIS*

for
CONSTIPATED ELDERLY

- Softens stools naturally without side-effects
- Promotes favorable intestinal flora
- Provides nutritive barley malt extract for under-par patients

2 FORMS—Liquid and Powder
Dose: 2 Tbs. A.M. and P.M.

Borcherdt's MALT SOUP *Extract*

*Non-diastatic barley malt extract neutralized with potassium carbonate

SEND FOR SAMPLES
BORCHERDT COMPANY • 217 N. Wolcott Ave., Chicago 12, Ill.
In Canada: CHEMO-DRUG COMPANY LTD., Toronto

FOR OLDER PATIENTS... *Soothing Relief* IN CHRONIC URINARY INFECTIONS

Urolitia can be given over long periods . . . without toxicity, without irritation, without drug fastness . . . to keep the urine free from E. coli, S. albus, S. aureus. . . . Promptly soothes the irritated membrane while providing bacteriostasis.

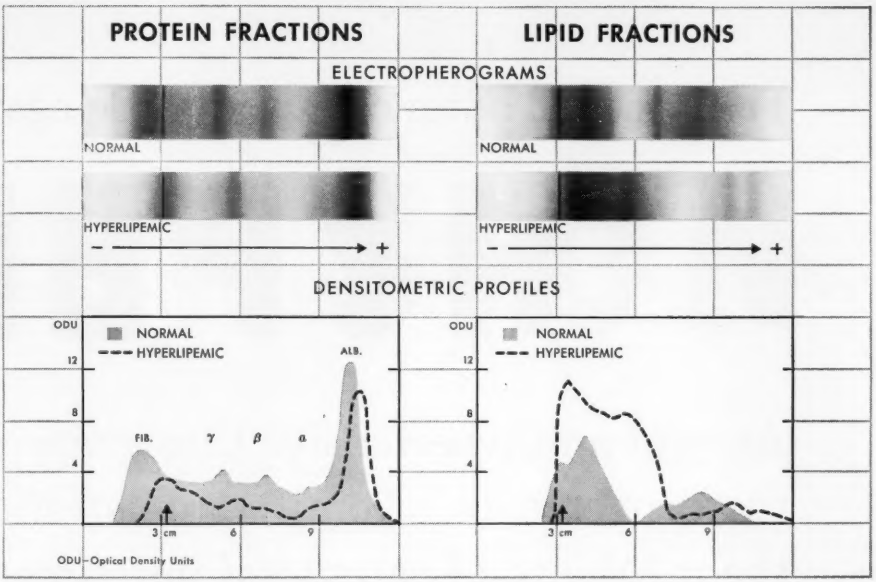
DOSE:
One tbs. in half cup warm water, q.i.d., ½ hr. a.c. and h.s.

Urolitia

METHENAMINE URINARY ANTISEPTIC

Sample on request

Cobbe Div., BORCHERDT MALT EXTRACT CO.,
217 N. Wolcott Ave., Chicago 12, Ill.



BLOOD DRAWS ITS OWN PROFILE

Here's one of the most ingenious methods of blood analysis! A small strip of paper in an electric field paints a picture that's worth a thousand calculations!

Principle: The phosphatides and phosphatide-containing complexes travel along the electrified path of the paper strip allowing identifiable protein and lipid complexes to be deposited at various points. Where the phosphatide content is insufficient, electroneutral lipids (cholesterol, neutral fat) are set free to remain at the starting point. Thus we obtain the characteristic tell-tale density zones of the electrophoretic profile.

Significance: Paper electrophoresis provides demonstrable physical evidence in disturbances of lipid metabolism and in associated disease states. Characteristic patterns have been obtained in hypercholesteremia, hyperlipemia, lipoid nephrosis, etc.; electrophoretic profiles from various species illustrate their relative predisposition to atherosclerosis.

Application: Paper electrophoresis is now being used to investigate the influence of dietary supplementation with "RG" Lecithin upon lipoprotein patterns in patients with lipid metabolism disturbances.

Glidden's "RG" Lecithin consists of 90% natural phosphatides in dry, free-flowing granules refined from soybeans. It is the only lecithin made expressly for medically indicated dietary purposes.

"RG" Lecithin is well tolerated and readily utilized by the body. *There are no contraindications.* Daily dietary supplement: 1 tablespoonful (7.5 Gm.) in juices or on cereals. (Up to 60 Gm. daily are used in clinical trials.)

Literature on lecithin in health and disease available on request.

Glidden QUALITY PRODUCTS

RG® LECITHIN A dietary phosphatide supplement.

The Glidden Company · Chemurgy Div., 1825 N. Laramie Ave., Chicago 39, Ill.

Fundamental advance in the battle against

HYPER

An oral antihypertensive that gives the convenience of oral administration, the reliability of parenteral injection

INVERSINE is a *totally new* antihypertensive agent. It is mecamylamine, a secondary amine, *chemically different* from all other ganglionic blocking agents.

INVERSINE is both *potent* and *reliable* on *oral* administration. It has been *proved therapeutically effective* in the treatment of hypertension, and has been used by many investigators on thousands of patients.

In one of many clinical trials,* "The over-all response rate was 92%, and 24% of the patients became normotensive." Investigators have found INVERSINE to be "... the most potent ... of the three drugs in reducing the blood pressure ..."[1] [INVERSINE and two other ganglionic blocking agents.]

Completely absorbed when it is given by mouth, INVERSINE "... has such a gradual onset and offset of action that a continuous and effective level of blockade can be readily achieved ..."[2]

INVERSINE *Provides Many Clinical Advantages.*

1. *Excellent reproducibility* of effects.

2. *Most potent* of all available oral ganglionic blockers (10 to 20 times more potent than pentolinium and about 90 times more potent than hexamethonium).

3. *Smooth, predictable response.* In a given patient, the same dose of INVERSINE elicits the same blood pressure response, time after time, *with minimal day-to-day fluctuation.*

4. *Remarkable physiologic economy* (because completely absorbed), resulting in *long duration of action, sustained effect.*

5. *Gradual* onset of effect.

6. *Small oral dosage* produces required hypotensive effect.

7. *Effective* even in patients refractory to hexamethonium and other ganglionic blocking agents.

INVERS

RTENSION

ADDITIONAL ADVANTAGES

When INVERSINE is used for ganglionic blockade, some patients suffering from hypertension may experience relief of pre-existing headache and angina pectoris.

Many patients with retinopathy, congestive heart failure and electrocardiographic abnormalities have shown signs of improvement during treatment with INVERSINE.

SIDE EFFECTS

INVERSINE (mecamylamine) is a very potent agent which must be used with care. Side effects observed during clinical use are due to excessive pharmacologic action, and may be minimized by careful adjustment of dosage and close supervision of the patient.

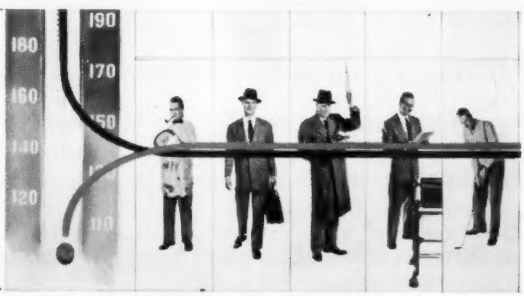
References:

1. Moyer, J. H., et al.: Drug Therapy of Hypertension: Preliminary Observations on the Clinical Use of Mecamylamine (A Ganglionic Blocking Agent) in Combination with Rauwolfia for the Treatment of Hypertension, Med. Rec. & Ann. 49:390 (Sept.) 1955.
2. Sturgis, C. C., et al.: Advances in Internal Medicine, J. Michigan M. Soc. 55:154 (Feb.) 1956.

*In this clinical trial all patients were given, in addition to one of the ganglionic blocking agents, a constant daily amount of reserpine.

INVERSINE is a registered trademark of Merck & Co., Inc.

The same dose
provides
the same results
...day after day

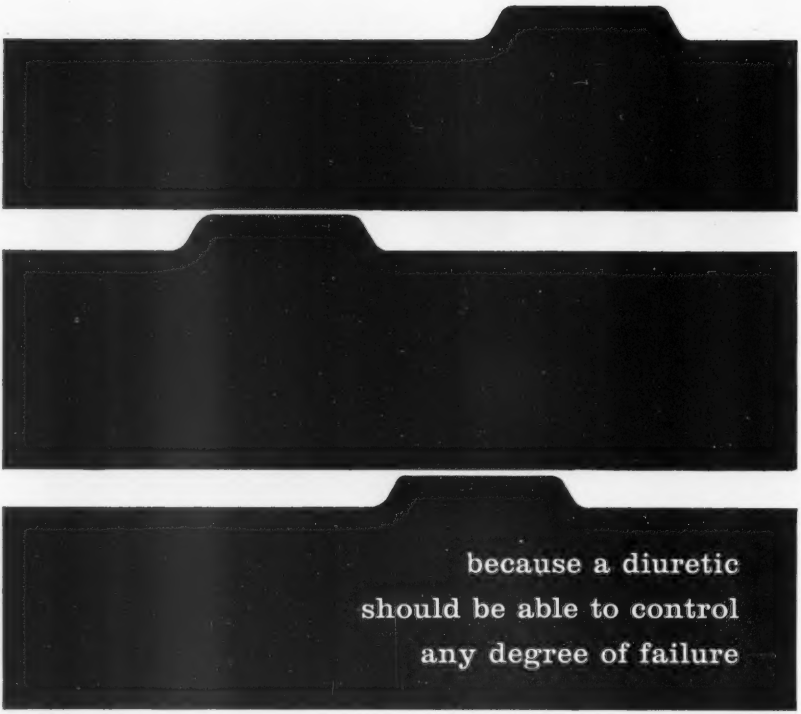


RSINE®

MECAMYLAMINE HYDROCHLORIDE

MSD

MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC.
PHILADELPHIA 1, PA.



PATIENTS IN FAILURE NEED AN ORGANOMERCURIAL

Certain diuretics are apt to mask the gradual onset of severe failure because they are effective only in the milder ambulatory cardiacs. The recurrent accumulation of fluid permitted by intermittent or arbitrarily limited dosage must eventually progress to more severe decompensation.

Because they can control *any* grade of failure, the organomercurials improve prognosis and prolong life.

TABLET

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Drug therapy of hypertension in the elderly patient

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The indications for definitive antihypertensive therapy are not dependent on the age of a patient but rather on the severity of the hypertension and the basic pathology. Close supervision of therapy and active treatment of untoward effects are essential if potent antihypertensive agents are used.

◆ Drugs that act to block impulses traveling over the autonomic nervous system are now available, making it possible to reduce blood pressure in hypertensive patients and to relieve associated symptoms. Although it is established that essential hypertension is a systemic vascular disease with certain symptoms and signs resulting from damage to many vascular beds, some authorities hold that reduction of blood pressure in the elderly patient is of no therapeutic value and is therefore irrational. It is important to determine whether this assumption is valid, for symptoms and signs attributable to the autonomic blocking agents themselves are common. In addition, antihypertensive therapy requires close medical supervision, since irreparable damage to the kidney or brain may result from excessive reduction of blood pressure. The objectives of this report are: (1) to evaluate the complications associated with diastolic hypertension in elderly patients, and (2) to compare the response to therapy of elderly patients with that of patients of all age groups with diastolic hypertension.

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Materials and Methods

We studied 97 patients with diastolic hypertension. All were 60 years of age or older, and all had been treated as out-

patients with various antihypertensive drugs. The drugs chosen were those which have been found most efficacious for treatment of hypertension in the average hypertensive patient including all age groups. We analyzed only patients with diastolic pressures over 100 mm. Hg. with respect to effectiveness of blood pressure control, side effects from the drug, and improvement in clinical manifestations resulting from untreated hypertensive vascular disease. We included five groups of patients: (1) 346 average hypertensive patients and 34 elderly hypertensive patients who received Rauwolfia alone; (2) 25 average hypertenstive patients and 12 elderly hypertensive patients who received Rauwolfia plus veratrum (protoveratrine); (3) 15 average hypertensive patients and 14 elderly hypertensive patients who received Rauwolfia plus hydralazine; (4) 75 average hypertensive patients and 17 elderly hypertensive patients who received Rauwolfia plus pentolinium; and (5) 80 average hypertensive patients and 20 elderly patients who received Rauwolfia plus mecamylamine.

Prior to therapy, all patients were evaluated carefully with respect to preliminary history and physical examination; complete blood count; electrocardiogram; blood urea nitrogen determinations; chest roentgenograms; urinalysis; and, in some cases, Fishberg concentration tests or phenolsulphonphthalein excretion tests. At each clinic visit, a brief history was taken and physical examination was made, in addition to weight, temperature, blood pressure, and pulse rate determinations. The control observations are the average of all blood pressure and pulse rate determinations during the first four clinic visits. During this time only placebos were given. After the control blood pressures and pulse rates were established, the patients were started on antihypertensive medication. On following weekly visits, increments were made in the dosage of those patients who were taking veratrum, hydralazine, pentolinium, or mecamylamine, until an adequate blood pressure response was obtained, or until side effects or complications of therapy either prohibited further increase of dosages or necessitated termination of therapy.

It was not necessary to titrate the dosage in those patients receiving Rauwolfia alone, as was the case in the patients who received the more potent drugs. Instead, these patients were placed on a standard dose of either 1 mg. of reserpine a day, or 4 mg. of alseroxylon a day, or 300 mg. of the whole root. In order to evaluate more adequately the patients in each treatment group, they were further subdivided on the basis of the degree of elevation in diastolic blood pressure during the control period. The patients with a control upright diastolic blood pressure greater than 100 but less than 120 mm. Hg were placed in subgroup A, and those patients with a control diastolic blood pressure greater than 120 mm. Hg in subgroup B.

The post-drug observations are the average of all blood pressure and pulse rate determinations after the titration period—the period during which the effective drug dosage was established and the blood pressure stabilized. In patients receiving Rauwolfia alone, the post-drug observations were made two weeks after the start of therapy. A response to any method of therapy was considered as a drop in the mean blood pressure (diastolic blood pressure plus one-third of the pulse pressure) of 20 mm. Hg or more in the upright position. A patient was considered normotensive if the blood pressure was reduced to, or below, 150/100 mm. Hg in the upright position.

Table 1 summarizes the vital statistics and incidence of complications of hypertension prior to therapy as found in 541 average hypertensive patients, including all therapeutic groups, and in 97 patients

over 60. The number of men and women was about equal in the average hypertensive group, whereas in the group of elderly patients over 60, women predominated about 2 to 1.

The incidence of renal damage and electrocardiographic abnormalities was slightly higher in the elderly patients. Otherwise, there was no basic difference between the incidence of complications in the two groups. The relative severity of the hypertensive vascular disease is obvious when incidence of complications associated with hypertension in these patients is rated. Therefore, if reducing blood pressure is effective in arresting or improving complications caused by hypertension, it should be effective in both groups included in this study. We conclude from these data that complications associated with hypertension are as likely to occur in patients of all ages as they are in patients over 60. Such observations are surprising, for it would be expected that incidence and severity of complications secondary to hypertensive vascular disease would be higher in older patients, because of the longer duration of the hypertension.

TABLE 1

VITAL STATISTICS AND INCIDENCE OF COMPLICATIONS OF HYPERTENSION PRIOR TO THERAPY

	Average patient	*Elderly patient*
Number patients treated	541	97
Average age	52 years	65 years
	Percentage of those treated	
Males	45%	35%
Females	55%	65%
White	26%	32%
Negro	74%	68%
Renal disease*	31%	51%
Cardiac failure	41%	44%
Angina pectoris	14%	15%
Electrocardiographic abnormality†	63%	80%
Cerebral vascular accident	23%	19%
Fundi‡		
1+ or 2+	74%	81%
3+ or 4+	16%	14%

*Varies from proteinuria to fixed specific gravity of the urine and elevated blood urea nitrogen.

†Varies from nonspecific T-wave changes to left ventricular hypertrophy.

‡Keith-Wagener-Barker classification.

Results

For analysis, we shall consider each method of therapy separately, and compare each group of elderly patients to the average patients receiving the same therapy. At the same time, we shall try to compare results in patients with milder diastolic hypertension (diastolic blood pressures between 100 and 120 mm. Hg) with results in those patients with more severe disease (diastolic pressure above 120 mm. Hg).

RAUWOLFIA ALONE

Table 2 presents the blood pressure response to therapy in patients who received Rauwolfia alone. Of the 346 average patients, the over-all response rate—that is, more than 20 mm. Hg reduction in mean blood pressure—was 53 per cent. The normotensive rate was 25 per cent. In contrast, there was a response rate of 41 per cent in the elderly patients, and of these, 9 per cent became normotensive. Thus the response rate to Rauwolfia in patients over 60 was not quite as good as in the larger group of average patients. Patients in the elderly group with more severe disease—that is, diastolic pressure of 120 mm. Hg before treatment—exhibited a better response than did the patients in the less severe group.

Incidence of improvement in symptoms and signs following antihypertensive therapy is shown in table 3. Over 50 per cent of the patients in both groups, who complained of headaches prior to therapy, obtained relief. Similarly, improvement of angina pectoris occurred in about one-third of the patients in both groups. Congestive heart failure was prominent in a high percentage of patients in both groups, but the

TABLE 2

BLOOD PRESSURE RESPONSE TO FIVE DIFFERENT METHODS OF THERAPY

Therapy	Average patients			Elderly patients		
	Subgroup A*	Subgroup B†	Total	Subgroup A*	Subgroup B†	Total
Rauwolfia alone						
Number treated	187	159	346	16	18	34
Per cent responsive‡	51	55	53	31	50	41
Per cent normotensive‡	35	14	25	13	6	9
Rauwolfia + veratrum						
Number treated	14	11	25	7	5	12
Per cent responsive‡	36	55	44	43	80	58
Per cent normotensive‡	21	0	12	14	0	8
Average dose‡ protoveratrine of responsive patients	2.2 mg.	3.7 mg.	3.0 mg.	2.4 mg.	2.6 mg.	2.5 mg.
Rauwolfia + hydralazine						
Number treated	3	12	15	4	10	14
Per cent responsive‡	33	100	87	100	80	86
Per cent normotensive‡	33	33	33	25	0	7
Average dose‡ hydralazine of responsive patients	200 mg.	342 mg.	331 mg.	213 mg.	301 mg.	271 mg.
Rauwolfia + pentolinium						
Number treated	20	55	75	3	14	17
Per cent responsive‡	70	82	79	100	86	88
Per cent normotensive‡	30	35	33	0	29	24
Average dose‡ pentolinium of responsive patients	248 mg.	358 mg.	332 mg.	222 mg.	292 mg.	275 mg.
Rauwolfia + mecamylamine						
Number treated	15	65	80	5	15	20
Per cent responsive‡	80	97	94	60	100	90
Per cent normotensive‡	33	38	38	20	60	50
Average dose‡ mecamylamine of responsive patients	18 mg.	27 mg.	25 mg.	19 mg.	25 mg.	22 mg.

*Control upright diastolic blood pressure > 100 mm. Hg but < 120 mm. Hg.

†Control upright diastolic blood pressure > 120 mm. Hg.

‡Key to terms:

Responsive—a drop in the upright blood pressure (mean) of 20 mm. Hg or more.

Normotensive—an upright blood pressure of 150/100 mm. Hg or less.

Average dose—average dose given in a twenty-four-hour period.

percentage of patients improving with Rauwolfia alone was higher in the elderly patients. However, there was a relatively small number of patients in this group which may account, in part, for this finding. Funduscopic changes, renal vascular changes, and electrocardiographic abnormalities responded poorly to Rauwolfia alone. This may be because these changes were, in a large part, caused by arteriosclerosis, rather than directly by the hypertension; and, if they were caused by hypertension, the reduction in blood pressure was not very dramatic; thus, reversal of these effects was not very evident. A reduction in pulse rate of more than 10 beats per minute was not so frequent in the elderly patients as it was in the average patients, occurring in 38 and 65 per cent of patients respectively.

Side effects from Rauwolfia were about the same in both groups as shown

TABLE 3

THE BENEFICIAL EFFECTS OF ANTIHYPERTENSIVE THERAPY

	Brady-crotic response*	*Headache*	*Angina pectoris*	*Con-gestive heart failure*	*Electro-cardio-graphic abnor-mality*	*Renal damage*	*Fundu-scopic changes*	*Roent-geno-graphic changes*
Rauwolfia alone								
Average patients								
Number with symptom	346†	142	45	128	208	65	38	100
Per cent improved	65	70	38	16	7	0	5	—
Elderly patients								
Number with symptom	34†	16	7	13	27	14	34	9
Per cent improved	38	50	29	54	15	0	0	22
Rauwolfia + veratrum								
Average patients								
Number with symptom	25†	11	4	7	19	15	23	11
Per cent improved	44	64	75	28	66	14	—	0
Elderly patients								
Number with symptom	12†	9	1	3	9	9	9	5
Per cent improved	75	78	100	0	33	17	—	—
Rauwolfia + hydralazine								
Average patients								
Number with symptom	15†	4	1	8	12	9	5	11
Per cent improved	73	50	0	13	8	11	20	0
Elderly patients								
Number with symptom	14†	6	2	11	12	6	11	6
Per cent improved	43	67	0	9	8	17	9	0
Rauwolfia + pentolinium								
Average patients								
Number with symptom	75†	23	7	23	52	8	12	58
Per cent improved	67	78	71	65	40	37	58	38
Elderly patients								
Number with symptom	17†	6	2	8	13	9	14	6
Per cent improved	59	67	0	38	15	0	0	50
Rauwolfia + mecamylamine								
Average patients								
Number with symptom	80†	52	10	27	67	61	17	48
Per cent improved	49	71	80	81	25	25	59	31
Elderly patients								
Number with symptom	20†	14	3	8	17	11	18	9
Per cent improved	35	57	100	75	45	45	11	45

*A decrease in the pulse rate of 10 beats per minute or more.
†Indicates number of patients in series.
—Data not available.

in table 4. Increased appetite, nasal congestion, sedation, and a sense of well-being were the outstanding manifestations. Inability to sleep at night was seen frequently in patients who received Rauwolfia for a prolonged period; this manifestation tended to be more severe in older patients. However, a direct correlation with this side effect and age was not evident.

RAUWOLFIA PLUS VERATRUM

This combination provided a comparable response rate in 12 elderly hypertensive

TABLE 4

SIDE EFFECTS OF FIVE METHODS OF DRUG THERAPY OF HYPERTENSION
(EXPRESSED IN PER CENT OF PATIENTS RECEIVING TREATMENT)

	Rauwolfia alone		*Rauwolfia + veratrum*		*Rauwolfia + hydralazine*		*Rauwolfia + pentolinium*		*Rauwolfia + mecamylamine*	
	*A.P.**	*E.P.†*	*A.P.**	*E.P.†*	*A.P.**	*E.P.†*	*A.P.**	*E.P.†*	*A.P.**	*E.P.†*
Number patients treated	346	34	25	12	15	14	75	17	80	20
	%	%	%	%	%	%	%	%	%	%
Increased appetite	54	29			20	43	32	18	23	15
Nasal congestion	64	59	24	33	53	57	51	35	33	25
Sedation	48	38			33	29	39	24	56	60
Dizziness	12	18	16	25	47	43	40	41	45	50
Sense of well-being	43	20							18	10
Weakness	23	29	32	42	73	79	66	71	46	30
Constipation			4	8	7	29	49	41	69	75
Nausea and vomiting			64	67	20	29			3	
Palpitations					7	36			6	
Angina					7	14			1	
Headache					7	57				
Blurred vision			24	8					43	35
Dry mouth			8	17					41	45
Syncope							1		5	5

*A.P.—Average patients. †E.P.—Elderly patients.

patients and 25 average hypertensive patients thus treated—58 per cent in the former and 44 per cent in the latter. Table 2 shows that a greater percentage of patients with control diastolic blood pressures greater than 120 mm. Hg responded to this regimen than was seen in patients with less severe disease. This held true for the average as well as for the elderly patient. Few patients in either age group returned to normotensive levels. The dose of veratrum in this study was slightly lower in the elderly than in the average patient.

Incidence of symptomatic improvement with Rauwolfia and veratrum therapy was similar in both age groups (table 3). However, improvement in electrocardiographic abnormalities was observed in twice as many average as elderly patients, and nearly twice as many elderly patients obtained a bradycrotic response. This is in direct contrast to Rauwolfia and hydralazine therapy in which a bradycrotic response was obtained in a greater percentage of average patients. This discrepancy may be attributed to the small number of patients in both studies rather than to a true difference in response to the two drugs. None of the three elderly patients with heart failure showed improvement, whereas a small percentage of average patients with heart failure was improved.

The majority of patients receiving Rauwolfia and veratrum had side effects of nausea and vomiting (table 4). Sixty-seven per cent of the elderly and 64 per cent of the average hypertensive patients were bothered by these symptoms at some time during therapy. In these patients, it was found necessary to titrate the dosage of veratrum to the emetic level to lower the blood pressure. When the emetic level was reached, the dosage of veratrum was reduced slightly and the patients were maintained on this dosage. In 33 per cent, an adequate blood pressure response was obtained before the emetic dose was reached. Dizziness was experienced by one-fourth of the elderly and by about one-sixth of the average

patients. Other side effects, which may have been due to veratrum, were not significant.

RAUWOLFIA PLUS HYDRALAZINE

Use of Rauwolfia plus hydralazine in the elderly patients produced a response rate of 86 per cent, but only one patient returned to normotensive levels (table 2). The blood pressure response in patients with less severe disease was about the same as in those with more severe disease. Among the average patients, the response rate was lower in patients with milder hypertension. However, the overall response rate was essentially the same in the elderly as in the average patients, although the normotensive rate was lower in the older patients. The average dose of hydralazine in the responsive patient was slightly greater in the average group than in the older group.

Incidence of symptomatic improvement in the older patients was approximately the same as that of the average patients (table 3). Here again, headache was relieved in over 50 per cent of patients receiving such combined antihypertensive therapy. Angina pectoris was not improved, and congestive heart failure only rarely. This was to be expected, for hydralazine produces some cardiac stimulation through its effect on the sympathetic nervous system. Interestingly enough, with this drug combination, 43 per cent of the elderly patients and 73 per cent of the average patients obtained a bradycrotic response, in direct contrast to patients who received hydralazine alone. In these patients, a bradycrotic response was rare, whereas tachycardia and palpitations were frequent. This is, in itself, the chief indication for giving Rauwolfia with hydralazine.

Incidence of side effects was essentially the same in the average as in the elderly patient, except that palpitations, headaches, and angina were considerably more frequent in the elderly than in the average patient. Increased appetite, nasal congestion, sedation, dizziness, weakness, and nausea were seen frequently in all groups of patients receiving this combination. It was necessary to discontinue therapy in one elderly patient, because of the severe side effects from hydralazine.

There is a paradox in this group of patients. Although headaches were prominent side effects of Rauwolfia plus hydralazine, at the same time, lowering of the blood pressure improved the headaches caused by hypertension in 67 per cent of the elderly and 50 per cent of the average patients who had these complaints before therapy. Thus, the majority of elderly patients with headaches from hypertension showed improvement with therapy. About one-half of the patients experienced headaches as a side effect at some time during therapy.

RAUWOLFIA PLUS PENTOLINIUM

Combination of Rauwolfia plus a ganglionic blocking agent, pentolinium, proved to be an effective antihypertensive measure. Among the elderly patients, 88 per cent showed a significant reduction in blood pressure, and 79 per cent in the average group reacted similarly (table 2). Twenty-four per cent of the older patients became normotensive, as compared to 33 per cent of the average group. The dose requirement in the older patients was slightly lower than in the average patients. All of the older patients who became normotensive were from the group with more severe disease —that is, pretreatment diastolic blood pressure above 120 mm. Hg. This may be ascribed to the small group of patients in subgroup A.

A bradycrotic response was seen in 59 per cent of the older patients as shown in table 3. Improvement was shown in 67 per cent of the patients with hypertensive headaches, in 38 per cent of those with congestive heart failure, and in 15 per cent of those with electro-

cardiographic abnormalities. Improvement in cardiomegaly, noted on roentgenographic examination, was seen in about one-half of the patients from both groups with this finding.

Side effects were virtually the same in the elderly as in the average patients (table 4). Constipation, caused by blockade of the parasympathetic ganglia, was present in 41 per cent of the older and in 49 per cent of the average patients. Weakness was a prominent complaint of 71 per cent of the elderly patients, and 41 per cent were dizzy at some time during therapy. Other side effects listed, except syncope, were caused by the Rauwolfia.

RAUWOLFIA PLUS MECAMYLAMINE

The response rate to this combination was somewhat better in the average group than with Rauwolfia plus pentolinium—that is, 94 per cent as compared to 79 per cent (table 2). However, the normotensive rate was practically the same. The response rate in the elderly group was also about 90 per cent—patients with more severe disease showing a slightly greater rate than those with milder disease. The normotensive response rate in this group was about 50 per cent. The dose requirement of mecamylamine was similar for all groups although slightly greater in patients with more severe disease. This held true for both elderly and average patients. Age did not appear to affect dose requirement of mecamylamine significantly.

Bradycrotic response and improvement in headache and funduscopic examination were observed in a smaller percentage of the elderly than of average patients (table 3). Angina pectoris was improved in all three of the elderly patients who had this complaint prior to therapy. Of those with congestive heart failure, 75 per cent of the elderly and 81 per cent of the average patients were improved during therapy. There was a slightly higher percentage of patients showing electrocardiographic improvement among the older than among average patients.

Constipation, the most common side effect, was present in 75 per cent of elderly patients, and was pronounced in 10 per cent. Blurred vision was experienced by 35 per cent of the elderly patients, weakness by 30 per cent, and dizziness by 50 per cent. Only one elderly patient experienced actual syncope. Forty-five per cent complained of dry mouth. The other side effects were caused by Rauwolfia rather than by the ganglionic blocking agent. Most of the side effects were present in about the same percentage of both age groups. Weakness, blurred vision, nasal congestion, and increased appetite were less common in the elderly patients, but constipation was slightly more frequent.

Discussion

When we compare the complications of hypertension in the 97 elderly patients to those of 541 average patients, it is obvious that the only significant difference is the higher incidence of electrocardiographic abnormalities and renal damage in the older patients. Eighty per cent of elderly patients had electrocardiographic abnormalities, compared with 63 per cent of the average patients. The other complications of hypertension were present in essentially the same percentage in both age groups. When we try to determine whether the more potent agents are indicated in the older age group with more severe hypertension, the similarity of the incidence of complications in the two age groups becomes very important. The major indication for antihypertensive therapy is a significant elevation of diastolic blood pressure, regardless of age. The elderly hypertensive patient with significant elevation in diastolic blood pressure should not be denied the benefit of more potent agents because

MEAN BLOOD PRESSURE

RESPONSE TO THE FIVE

THERAPEUTIC REGIMES EXPRESSED

IN PER CENT OF CONTROL

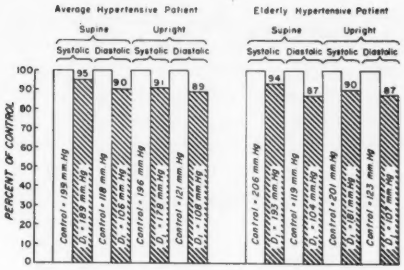

FIG. I. *Response to Rauwolfia alone.*

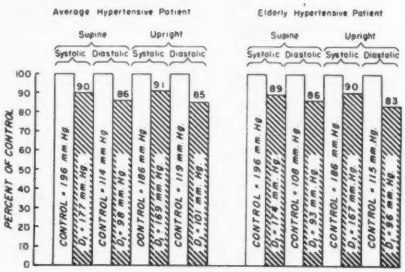

FIG. II. *Response to Rauwolfia plus veratrum.*

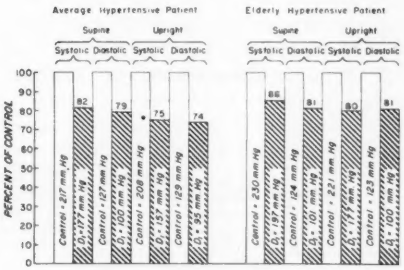

FIG. III. *Response to Rauwolfia plus hydralazine.*

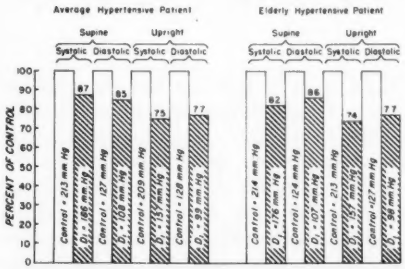

FIG. IV. *Response to Rauwolfia plus pentolinium.*

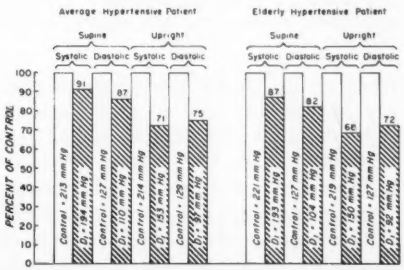

FIG. V. *Response to Rauwolfia plus mecamylamine.*

of his age. A careful study of the individual patient before therapy makes it easier to decide which therapy is best, and which complications may arise from such therapy.

Rauwolfia will reduce blood pressure in the elderly patient, just as it does in the average patient. The blood pressure response for both groups of patients receiving Rauwolfia is shown in figure I. The over-all reduction in blood pressure was almost identical for average and for elderly hypertensive patients. The average blood pressure response of the 12 elderly patients was essentially similar to the response of 25 average patients

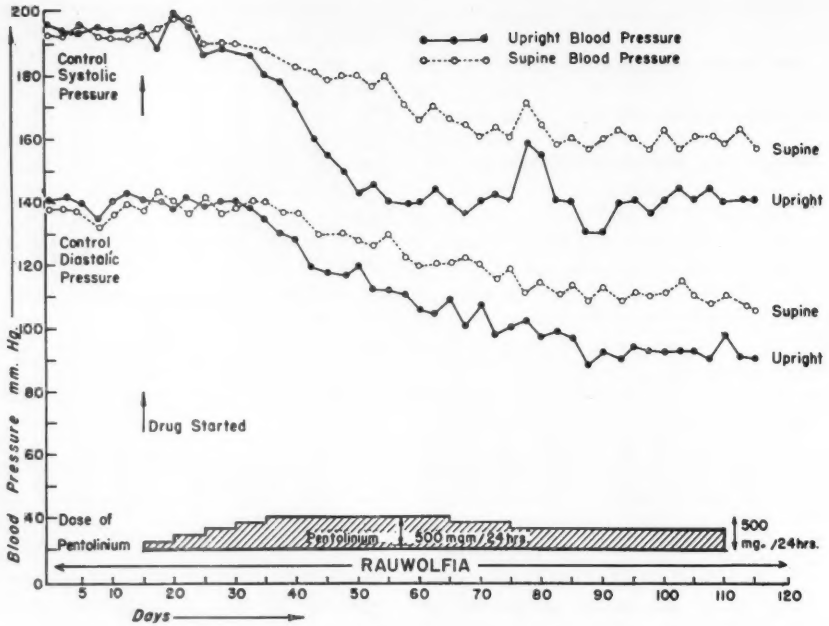

FIG. VI. *The response of blood pressure to Rauwolfia was inadequate in this patient with an elevation of the diastolic blood pressure above 120 mm., Hg; therefore, after five weeks, pentolinium was added and Rauwolfia continued. The dosage of the pentolinium was titrated until the upright blood pressure was near normotensive levels.*

receiving Rauwolfia plus veratrum (figure II), as was also true of the two groups treated with Rauwolfia plus hydralazine (figure III). There was some orthostatic effect on the blood pressure, which was greater in the average patient.

The response of the elderly patient to Rauwolfia combined with a ganglionic blocking agent was the same as in the average patient, but the dosage requirement of the drug was slightly lower in the older patient. Figures IV and V compare the reduction in blood pressure in patients who received Rauwolfia plus one of the ganglionic blocking agents. Response to Rauwolfia plus pentolinium and Rauwolfia plus mecamylamine was virtually identical in both average and elderly hypertensive groups. Complications, such as syncope and rising blood urea nitrogen, which appear occasionally when ganglionic blocking agents are used, were not more frequent in the older age group than in the average age group. However, these problems which require strict individualization are not necessarily determined by age, but by the underlying pathology present in each patient. Similarly, the beneficial effects of antihypertensive therapy are seen in the elderly patients, just as in the average patients, and present a direct response to blood pressure reduction. Obviously, reduction in blood pressure is not a cure for the disease, but such reduction does relieve many of the symptoms caused by hypertension and benefits many of the changes which occur as a result of hy-

pertension. This appears to be true in the average as well as in older patients with a persistent elevation in the diastolic blood pressure.

Recommendations for Treatment

Analysis of the preceding data indicates that the elderly patient with an elevation of diastolic blood pressure may be treated just as the average hypertensive patient. The same precautions should be taken, and the patient must be followed closely, particularly if the more potent ganglionic blocking agents are used. Patients must return at regular intervals for follow-up, and drug dosage must be titrated slowly and with great care. Figure VI shows our method for dose titration of the ganglionic blocking agents. Rauwolfia is always used in combination with the ganglionic blocking agents, and is given for five days to one week or more before beginning therapy with the ganglionic blocking agent. This reduces the requirement of the blocking agent, and produces a more constant blood pressure response. The initial dose of pentolinium—20 to 40 mg., given after breakfast and after supper—is increased progressively, at weekly intervals, until the blood pressure has been reduced to the desired level. Figure VI also demonstrates one of the problems that is almost invariably associated with ganglionic blocking agents—the orthostatic effect. Because of the nature of this drug, blood pressure reduction is greatest in the upright position. Despite this, beneficial effects are experienced, since the patient is usually upright for sixteen to eighteen hours each day. A greater reduction at night can also be maintained if the patient is directed to elevate the head of his bed at night, on 6- to 8-inch blocks.

Table 5 presents our therapeutic program for the treatment of the elderly patient with diastolic hypertension. Antihypertensive therapy is not given to the elderly patient with an elevation of systolic blood pressure, but is directed to the patient with a diastolic blood pressure of 100 mm. Hg or more. In patients with diastolic pressures between 100 and 120 mm. Hg, Rauwolfia is given ini-

TABLE 5

THERAPEUTIC APPROACH TO THE ELDERLY PATIENT WITH HYPERTENSION

Severity of hypertension	*Initial therapy*	*Adjunctive therapy**
Systolic blood pressure elevation, diastolic blood pressure < 100 mm. Hg	None	None
Diastolic blood pressure > 100 mm. Hg but < 120 mm. Hg	Rauwolfia†	Rauwolfia† + hydralazine** or Rauwolfia† + veratrum
Diastolic blood pressure > 120 mm. Hg.	Rauwolfia† for 1 to 2 months	Add pentolinium‡, hexamethonium‡ or mecamylamine‡
Severe progressive hypertension	Rauwolfia† plus ganglionic blocking agent‡ from the onset	

*Adjunctive therapeutic agent to be added to the regimen if the initial therapeutic agent is found to be inadequate.

**Start on doses of 25 mg. with each meal and at bedtime, adding 25 mg. for each dose weekly to a maximum of 600 mg. per day.

†4 mg. alseroxylon (Rauwiloid), 300 mg. crude root, or 1 mg. of reserpine per day.

‡Start in small doses and slowly increase the dose as indicated by the response in the standing position. The initial oral dose of hexamethonium is 125 mg. after each meal and at bedtime; of pentolinium, 20 mg. after each meal and at bedtime; and of mecamylamine, 2.5 mg. after breakfast and supper. The dose of these agents is progressively increased at weekly intervals until the desired blood pressure is obtained in the standing position.

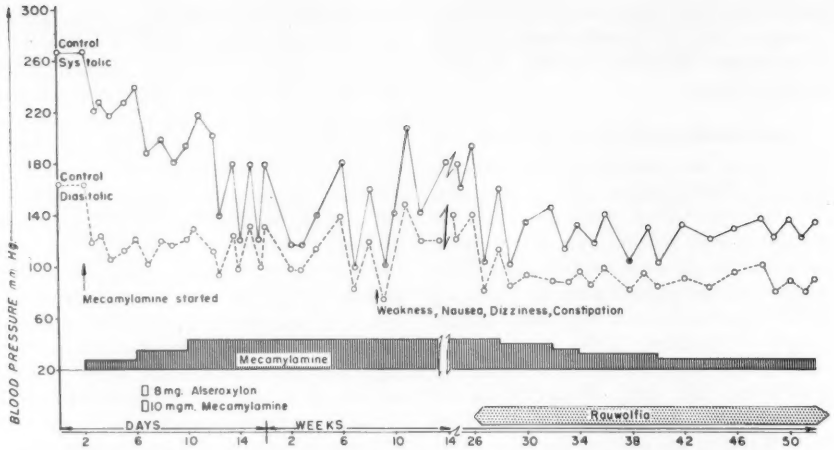

FIG. VII. *When the ganglionic blocking agent, mecamylamine, was given without concomitant Rauwolfia, this patient exhibited pronounced fluctuation in blood pressure response, even after the completion of titration and establishment of a fixed dosage. This resulted in hypotensive episodes producing nausea, vomiting, weakness, dizziness, and constipation. The addition of Rauwolfia to the therapeutic regimen permitted a more constant blood pressure effect with fewer and less significant blood pressure fluctuations and also permitted a reduction in the dosage of the ganglionic blocking agent. (Courtesy A.M.A. Arch. Int. Med.)*

tially and either hydralazine or veratrum is added if the desired response to Rauwolfia is not obtained. Rauwolfia is less effective in the elderly patient than in the average hypertensive patient, but apparently the incidence of symptomatic improvement is about the same in this group as in patients with more severe disease. Veratrum may be effective in the older patients, and may be very useful if adequate blood pressure response can be obtained without emesis. If this is inadequate, and a more potent antihypertensive therapy is indicated, the patient should be given Rauwolfia in conjunction with a ganglionic blocking agent such as mecamylamine or pentolinium. It must be emphasized again that the dose of the ganglionic blocking agent must be titrated carefully. The results which can be anticipated on this basis appear to make antihypertensive therapy in the elderly patient quite justifiable. The stabilizing effect of Rauwolfia on the blood pressure response to ganglionic blocking agents is well demonstrated in figure VII. In this patient, there was a very variable response to mecamylamine. When Rauwolfia was added, there was a significant reduction in dosage requirement of mecamylamine, and the patient's blood pressure became much more stabilized.

When any hypertensive therapy is used, the dose of the drug which causes optimal blood pressure response in the individual patient is relatively fixed. Therefore, if the patient's response to his environment varies during the period of antihypertensive therapy, one may expect a variable blood pressure response. Thus, it is desirable to maintain environmental circumstances as constant as possible. Figure VIII shows the blood pressure response in a patient who was relatively well controlled with mecamylamine therapy. When he was subjected to difficult business situations, ex-

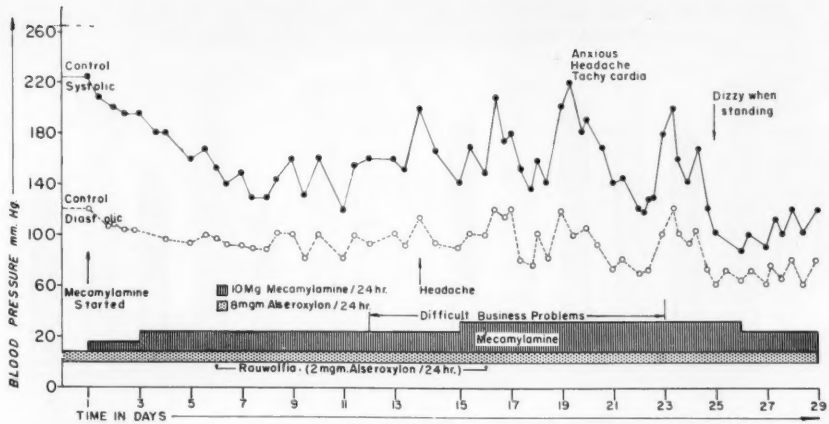

FIG. VIII. *After a fairly constant dose of mecamylamine had been established, this patient encountered excessive environmental stresses. This resulted in increased sympathetic outflow from the central nervous system manifested by elevation of blood pressure, headaches, tachycardia, and anxiousness. After these problems had been resolved, a smaller dose of the ganglionic blocking agent was required to control the blood pressure. (Courtesy A.M.A. Arch. Int. Med.)*

cessive rises in blood pressure were produced, resulting in a return of hypertensive symptoms. It was necessary to increase the dose of the blocking agent. Despite this, he continued to b r e a k through under periods of stress because of the increased number of vasoconstrictor impulses flowing out over the sympathetic nervous system. When his business difficulty was eradicated, the required dose of the drug was reduced, and an excessive drop in blood pressure occurred.

Excessive drops in blood pressure must be avoided, especially in patients with severe renal disease. If the patient has a progressively rising blood urea nitrogen, his drug dosage should be decreased or perhaps discontinued. The symptoms must be evaluated carefully at each visit. Table 6 presents the general degree to which blood pressure can be reduced, depending upon the degree of renal damage. In patients without renal damage, blood pressure can be reduced to normotensive levels in the upright position, without producing significant impairment of renal function. However, in the patient with moderately severe to severe renal damage, blood pressure should not be reduced excessively or functional decompensation may result. It is paradoxical that effective reduction in the blood pressure will arrest progressive renal damage, but at the same time, some functional impairment may occur, resulting from a pressure that is not adequate for maintaining an adequate excretory pattern. Figure IXA demonstrates the renal hemodynamic response to mecamylamine in a patient in whom there was a moderate reduction in blood pressure. Under these circumstances, there was an insignificant

TABLE 6

APPROXIMATE DEGREE OF BLOOD PRESSURE REDUCTION THAT CAN BE ACCOMPLISHED

Blood urea nitrogen (Mg. %)	*Reduce upright blood pressure to:*
Normal	130-150/80-100
BUN 30 to 60	150-170/100-110*
BUN 60 to 100	180-190/110-120*
BUN 100	No reduction

*Do not reduce blood pressure further if BUN rises.

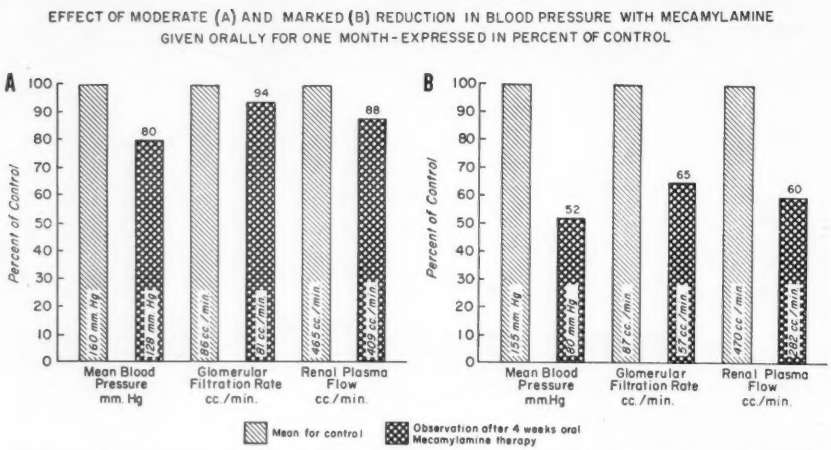

FIG. IX. A. *Moderate reduction in the blood pressure produces a slight reduction in renal function. (Courtesy A.M.A. Arch. Int. Med.)* B. *Excessive reduction of the blood pressure results in a significant depression of renal function.*

reduction in glomerular filtration rate. In contrast, figure IXB shows a significant reduction in glomerular filtration rate when the blood pressure was reduced to low normotensive levels (100/70). This patient had minimal renal damage. A reduction in renal function of this degree would be definitely contraindicated in a patient with severe renal damage. When excessive reduction in blood pressure occurs, the patient should be kept in the supine position, since the reduction in renal function that results from pronounced reduction in blood pressure is aggravated when the patient stands up.

Constipation should be treated actively with cathartics and prostigmine. This is a major side effect and fecal impactions or ileus may result if adequate relief measures are not taken. Milk of magnesia, in a dose of 15 to 30 cc., or cascara sagrada, in a dose of 10 to 15 cc., is usually adequate. If neither is adequate, combination of the two in the same dosages is given concurrently. Some patients do better with a dose of 15 to 30 mg. of prostigmine before each meal, which may be adequate to control the constipation. However, other patients will experience rather severe abdominal cramps and these do better with the cathartics. Trial and error is necessary to determine which method of combating the decreased bowel function is best suited to the individual patient.

Finally, the problem of early morning reactivity must be considered in the use of the longer acting ganglionic blocking agents, such as pentolinium and mecamylamine. We have found that when smaller doses are used for many of the older patients, they will do quite well with a dose of 2.5 to 5 mg. of mecamylamine, given after breakfast and after supper. However, as the daily dose requirement increases above 20 mg., early morning hypotension can be circumvented by giving a large dose at lunch, a moderately large dose at breakfast, and a smaller dose at supper, and none at bedtime. With this regimen the patient gets a more even distribution of the drug throughout the day, with the maximum effect obtained when he is exposed to maximum stress. If this is not done, the

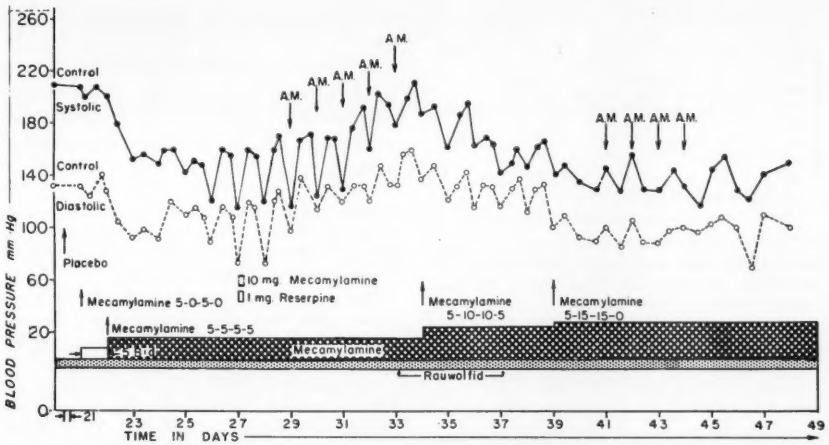

FIG. X. *Dose titration of mecamylamine showing dose adjustment, initial partial tolerance, and early morning reactivity. In patients receiving ganglionic blocking agents, who experience excessive reduction of blood pressure in the morning, adjustment of the dosage schedule is necessary. Decreasing or withholding the bedtime dose and giving a relatively large noon dose will allow a more constant effect. (Courtesy A.M.A. Arch. Int. Med.)*

patients gets an excessive drop in blood pressure on arising in the morning (figure X and table 7).

Hypertension in the elderly patient can be just as severe as hypertension in the younger patient. For example, the patient whose case is presented in figure XI had atherosclerosis of the aorta, with a complete occlusion of one renal artery. This resulted in a malignant hypertensive syndrome. This patient responded quite well to parenteral reserpine in a dose of 5 to 10 mg. every six hours for one week. Following this, the patient was placed on Rauwolfia plus the ganglionic blocking agent, mecamylamine. He is now doing quite well on the same medication. Thus, even for the elderly patient with malignant hypertension, treatment is essentially the same as for the younger patient.

Conclusions

1. A group of 541 average hypertensive patients was compared with a group of 97 patients over 60 years of age as to incidence of side effects associated with hypertensive therapy and response to antihypertensive agents.

2. Except for minor differences, such as a greater incidence of electrocardiographic abnormalities, a slightly greater incidence of cardiac failure, and a greater incidence of associated renal damage, the number of complications was essentially the same in the average hypertensive as in the elderly hypertensive patients.

3. The response to antihypertensive

TABLE 7

RENAL FUNCTION RESPONSE FOLLOWING HOMOGRAFT IN PATIENT WITH GOLDBLATT KIDNEY

	Glomerular filtration rate ml./min.		*Renal blood flow ml./min.*	
	*Right**	*Left*	*Right**	*Left*
Control	0	25	0	130
Blood pressure Rx.	0	35	0	200
Homograft				
1 month	0	45	0	425
6 months	0	60	0	725

*Occluded.

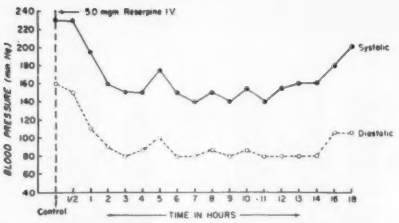

FIG. XI. *An elderly patient who developed malignant hypertension as a result of occlusion of the abdominal aorta and left renal artery was adequately controlled with parenteral reserpine until definitive surgery was carried out. As blood pressure control continued, renal function in the uninvolved kidney increased progressively. (Courtesy A.M.A. Arch. Int. Med.)*

measures was about the same in the elderly as in the average patients. With less potent agents, such as Rauwolfia and hydralazine, the response rate and normotensive rate were slightly less in the older patient. All in all, the response and indications for antihypertensive measures were essentially the same, regardless of age.

4. The therapeutic program for hypertension based upon results of our study, is applicable to the elderly hypertensive as well as to the average hypertensive patient.

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The various products used in this study were kindly supplied by the following pharmaceutical houses—alseroxylin (Rauwiloid) by Riker Laboratories, Inc.; reserpine, as Serpasil, by Ciba Pharmaceuticals and as Sandril, by Eli Lilly Company; protoveratrine as Veralba, by Pitman-Moore Company; hydralazine hydrochloride, as Apresoline, by Ciba Pharmaceuticals; pentolinium tartrate as Ansolysen, by Wyeth Laboratories, Inc.; and mecamylamine as Inversine, by Merck, Sharp and Dohme, Inc.

THE CANCER DEATH RATE in men has shown a significant increase during the past decade. Among men, the rate is now 13 per cent higher than for women 45 to 54 years of age; whereas, ten years ago, the rate for men was 11 per cent below that for women. At ages 55 to 64, the excess male mortality from cancer increased from 16 to more than 50 per cent.

Lung cancer has been largely responsible for the increased cancer mortality in men. The lung has far surpassed the stomach as the leading site of fatal cancers in middle-aged men. The death rate from pulmonary cancer rose to nearly three times the rate for cancer of the stomach, the next leading site, during the decade 1945 to 1955. Lung cancer now accounts for nearly 30 per cent of the total cancer mortality among men 45 to 64 years of age.

Women experienced a reduction of about one-third in mortality from uterine cancer. This encouraging result reflects the progress made by prompt diagnosis and early treatment.

Statist. Bull. Metrop. Life Insur. Co. 37: 1-4, 1956.

Electroconvulsive therapy

A controlled study of its effects in geriatric patients

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Thirty-six patients over 65 received mental tests and behavior ratings before and after a treatment period. A key group of 12 patients received electroconvulsive therapy and two control groups provided opportunity to compare and assess the effects of this form of therapy in people showing primarily the mental symptoms ascribed to senility.

◆ Electroconvulsive therapy, now nearing its third decade of use, has proved to be an important aid in treatment of affective illnesses. Advanced age, alone, is no longer felt to contraindicate its use where need is apparent. A review of pertinent literature leads to the conclusion that electroconvulsive therapy can be used in aged patients with eminent safety.[1-3]

Problems of Selection

The accepted indications for electroconvulsive therapy in emotional illnesses of the aged patient differ little, if at all, from those considered appropriate in younger age groups. Despite this helpful guidepost, selection of the responsive aged patient can be much more difficult, for his symptoms may represent a complex blend of organic, emotional, and attitudinal factors.

Rothschild found no significant relationships between symptoms and brain pathology in his study of necropsies performed on psychotic aged people.[4] Clow demonstrated the great importance of looking for emotional factors in aged patients presumed to be mentally ill as a result of organic brain disease.[5]

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These reports, among others, point up the need for critical appraisal of the term "irreversible," as it is applied to the symptoms of the aged patient. The authors' clinical observations and discussions with colleagues established that sometimes electroconvulsive therapy, given for other reasons, appears to ameliorate presumably irreversible symptoms.

It seems apparent that too little is known about the dividing line between that aged patient who might benefit from electroconvulsive therapy and the one who certainly will not benefit.

Purpose of the Study

The purpose of the study was to determine, under controlled conditions, the nature and degree of change in aged patients receiving electroconvulsive therapy. It was hoped that results of the study could be used in later investigations to define factors or symptoms

which would aid in better selection of the responsive aged patient.

Such definition is most important in state mental hospitals where the work-up period becomes much telescoped because of an increasing patient load. Conceivably, in these hospitals, less conservatism in prescribing electroconvulsive therapy might point more patients toward rehabilitation and fewer toward long custodial care.

Of necessity, the study group was comprised of patients with those mental symptoms which are generally regarded as the irreversible changes of age.

Design and Procedure

This group was selected from 113 patients over 65 who were admitted during a seven and one-half month period. Following a five- to ten-day observation period, those patients who seemed certain to respond favorably to electroconvulsive therapy were excluded. Also excluded were patients in precarious physical condition and those with rating difficulties, such as the blind, seriously deaf, aphasic, and so on. Thus, in selecting by exclusion, we eventually dealt with a study group composed of 18 men and 18 women. Average age of the group was 75 years.

All newly admitted patients over 65 received routine admission work-up and care including a dietary supplement of vitamins in therapeutic dosage.

DIAGNOSTIC CLASSIFICATION

Information about symptoms was obtained by sending a detailed inquiry form to persons who had attended each patient prior to hospitalization.

The percentages of the 36 study patients showing specific symptoms were as follows: memory failure, 83 per cent; failure to recognize familiar people or objects, 72 per cent; deterioration in self care, 64 per cent; noticeable suspiity, 61 per cent; changes in interest, ciousness, 61 per cent; changes in activ-58 per cent; increased irritability, 47 per cent; feelings of worthlessness, 28 per cent; sense of life being over, 28 per cent; threats or attempts to injure self, 22 per cent; grandiosity, 17 per cent; and threats or attempts to injure others, 14 per cent.

Standard systems of diagnosis were not used because of the relatively limited number of patients in the study. Instead, four symptom groups were designated after cataloguing the inquiry returns. These groups were:

S–Symptoms ascribed to senility only.
PD–Symptoms of paranoid and depressive character.
BS–Symptoms basically of senility but with some PD coloring.
BPD–Symptoms basically of PD character but with some senile coloring.

The frequency of these symptom entities within the study group was as follows: BS–17, S–7, BPD–9, PD–2, and unclassified–1.

The frequency of these symptom entities within the later determined treatment groups–that is, following random assignment–was briefly as follows: electroconvulsive therapy group–7 of the BS classification with 5 in other classifications; thiopental group–6 of the BPD classification with 6 in other classifications; placebo group–7 of the BS classification with 5 in other classifications.

PREPARATION FOR TREATMENT

During this phase, each patient's behavior was rated on the L-M scale.[6,7] Identical mental examinations were done, rating (1) orientation and applied memory, (2) auditory memory, and (3) visual memory. Blood pressure determinations were made. A rating based on clinical signs of arteriosclerosis was carried out according to method described by Gibson and Peckham.[8]

Following these pretreatment measurements, each patient was assigned at random to one of the three treatment groups.

RESULTS OF TREATMENT

		A (ECT)		B (Thiopental)		C (Placebo)	
		Men	Women	Men	Women	Men	Women
BLOOD PRESSURE READINGS							
Systolic pressure	Pre	170.3	166.0	181.6	162.3	150.3	155.3
	Post	+1.3	+2.1	−7.0	−27.7	+9.7	+4.0
Diastolic pressure	Pre	92.3	85.3	98.0	77.3	85.3	77.3
	Post	−5.5	−2.6	−10.0	−1.7	+7.0	+6.0
MENTAL TEST SCORES							
Orientation subtest	Pre	5.75	6.58	5.00	8.05	4.16	7.08
	Post	−0.83	−0.58	+0.92	+1.85	−0.91	+0.92
Auditory memory	Pre	1.17	3.66	0.83	3.17	2.33	3.17
	Post	+2.00	+0.34	+0.67	+1.13	−1.50	+0.33
Visual memory	Pre	3.50	2.16	1.33	3.00	0.83	2.83
	Post	−0.67	+0.84	+1.33	+1.00	+0.50	+1.17
Total test	Pre	3.48	4.05	2.42	4.68	2.40	4.30
	Post	+0.19	+0.27	+0.93	+1.40	−0.58	+0.70
BEHAVIOR RATINGS							
Work	Pre	1.33	1.17	1.25	1.20	1.08	1.25
	Post	−0.25	+0.16	+0.25	+0.80	+0.00	+0.17
Eating	Pre	2.06	3.08	2.66	3.25	2.33	3.58
	Post	−0.33	−0.13	+0.67	+0.37	+0.00	−0.25
Patients	Pre	2.83	3.00	3.00	3.10	2.67	2.75
	Post	+0.00	+0.04	−0.08	+0.20	+0.33	−0.17
Employees	Pre	2.25	2.88	3.25	3.16	2.08	2.67
	Post	−0.33	+0.20	+0.33	+0.94	+0.42	+0.25
Staff	Pre	2.92	2.83	3.00	3.13	3.00	2.83
	Post	+0.08	+0.09	+0.08	+0.07	−0.33	+0.17
OT & RT*	Pre	2.33	1.67	2.08	1.92	1.75	1.75
	Post	−0.40	+0.12	+0.22	+0.38	−0.17	+0.08
Dress	Pre	2.42	2.33	2.33	3.08	2.33	2.41
	Post	−0.72	−0.68	+0.58	−0.18	+0.17	+0.26
Psychomotor activity	Pre	3.20	2.83	3.25	3.00	2.83	2.83
	Post	+0.00	+0.47	+0.05	+0.20	+0.50	+0.33
Speech	Pre	2.92	3.75	2.67	4.00	2.83	3.33
	Post	−0.42	−0.96	+0.24	−0.40	+0.42	+0.00
Toilet	Pre	2.83	3.67	3.66	4.41	2.75	3.66
	Post	−0.33	−0.59	+0.09	−0.71	+0.33	+0.01
Average	Pre	2.51	2.72	2.72	3.03	2.37	2.71
	Post	−0.27	−0.13	+0.24	+0.17	+0.17	+0.09

*OT & RT refers to Occupational Therapy and Recreational Therapy.

TREATMENT

The treatment phase for each patient occupied three weeks. Two treatments were given weekly. Following a treatment, a patient went to a second room for recovery and to a third room for activities and refreshments.

The psychologist, Stuart Atkinson, and the treatment room staff were the only persons with accurate knowledge of what treatment any patient received. Other members of the staff had been instructed to give equal treatment to all study patients and to avoid open specu-

lation about treatments given. These instructions were well carried out.

Except for medication and electroconvulsive therapy, each patient received identical handling in the treatment room. He lay on the table, had jelly put on temples, had mouth gag inserted, and had electrodes applied. Further than this the specific treatments were:

Group A–Succinylcholine chloride intravenously with induction of grand mal seizure one minute later.

Group B–Thiopental intravenously in dosage sufficient to induce a ten-minute sleep–about 2.5 grains.

Group C–Sterile water intravenously with instructions that treatment might make the patient sleepy and, if so, he was to take a nap.

An effort was made to keep each patient, regardless of treatment type, in the treatment room for the same length of time.

STABILIZATION PERIOD

One month was allowed on the receiving ward for the dissolution of temporary effects of treatment. When this period had passed, the post-treatment evaluations of behavior, mental condition, and blood pressure were made.

FINAL ASSESSMENT

A month after leaving the receiving ward, the patient's behavior was again rated by personnel working on his new ward. Since most patients were transferred after completion of the stabilization period, this final behavioral rating came about two months after termination of treatment.

Results

BLOOD PRESSURE

Data on blood pressure determinations made before treatment and one month after termination of treatment are shown in the table. Only the direction and quantity of change is given in the post-treatment row.

Although decreases were seen in the group receiving thiopental, it was felt that over-all changes were not of practical significance.

MEMORY AND ORIENTATION

Data derived from the memory and orientation test are shown in the table. There were no changes of practical significance which could be assigned to the different treatments on any of the subtests. However, all groups showed a trend toward improvement on the total test scores. This trend reflects reliable improvement in visual memory in most groups.

BEHAVIOR RATINGS

Data from ratings of patients' behavior are also given in the table. The data show the pretreatment rating and the direction and amount of change when this rating is compared to that made thirty days after termination of treatment. The data derived from rating sixty days after treatment was so nearly identical to that of the thirty-day interval that no further comparative work was done with the former.

The three treatments do reflect a different effect on the average behavior of patients. The degree of these differences is of statistical but not of practical significance.

In general, it may be stated that patients receiving electroconvulsive therapy show a tendency toward deterioration in the measured area of behavior, while the control groups show a slight tendency toward improvement. Within the electroconvulsive therapy group, it appears that men are more vulnerable to the deteriorating effect than are women.

Those areas of behavior which appeared to deteriorate most under electroconvulsive therapy were habits of dress, toilet, speech, and eating.

OTHER RELATIONSHIPS

Relationships between the amount of sclerosis and changes in the patients' behavior and mental condition were determined by Spearman's rank difference correlation method.[9]

There was a reliable, though slight, relationship between the amount of sclerosis in the electroconvulsive therapy patients and the changes in their total mental test scores. The correlation coefficient of +0.61 indicates that the lesser the degree of sclerosis the more likelihood of the patient's showing improvement in these tests.

A reliable, though slight, relationship was found between sclerosis and changes in the average behavior of the electroconvulsive therapy patients. The coefficient, +0.61, indicated that the greater the degree of sclerosis, the greater would be the liability of behavioral deterioration under therapy.

Surprisingly, an opposite relationship (coefficient −0.58) appeared in the thiopental patients where a greater degree of sclerosis appeared to favor improvement.

It is of interest that the magnitude of improvement shown by the electroconvulsive therapy group in the total test score is less than that of the thiopental group and greater than that of the placebo group. In visual memory, the electroconvulsive therapy group shows the least improvement.

Also of interest is the fact that men's and women's visual memory is affected differently by different treatments. The visual memory of men shows slight impairment under therapy while women show slight improvement. Similarly, in the placebo group, women show more improvement in visual memory than men do.

Discussion

Perusal of the second and third tables reveals noteworthy differences between men and women patients. A potentiality for error existed here since necessity dictated that two different physicians select the candidates of each sex. It was felt that the degree of error, if any existed, could not be great since the principles of exclusion—therefore selection—were uniformly observed by the physicians assisting in the study. Therefore, certain probabilities seem worth mentioning. These are: (1) that aged women, as a group, have less mental impairment at the time of admission, (2) that women resist better than men the deteriorating effects of electroconvulsive therapy on critical faculties (see table), and (3) that women resist better than men the deteriorating effects of electroconvulsive therapy on behavior in general.

Behavioral regression is implicit in the use of electroconvulsive therapy in any age group, but this, of course, depends on the frequency and the extent to which it is used. This tendency in its incipiency in an aged patient group is apparent in the present study. None of our patients on therapy became real problems in care because of behavior deterioration, yet the trends noted are in this direction and are near a degree of practical significance. It is probable that giving the six treatments at more frequent intervals or giving more than six treatments at the same intervals would have resulted in notable deterioration in mental faculties and behavior.

Conclusions

A group of 36 patients, consisting of 18 men and 18 women past 65, were selected from new admissions to Fergus Falls State Mental Hospital. The majority showed mental symptoms ascribed to late processes of aging. They were given certain mental examinations, behavioral ratings, and clinical determination of blood pressure and degree of sclerosis.

Twelve were given electroconvulsive therapy; 12 thiopental; and 12 intrave-

nous sterile water in a treatment schedule otherwise identical and which occupied three weeks of time. One month subsequent to treatment, the same tests were given.

Electroconvulsive therapy did not significantly alter blood pressure; it slightly improved memory-orientation faculties as measured by mental test scores; and it produced statistically significant deterioration in behavior which was most noticeable in areas of dress, toilet, speech, and eating. Women appeared to be less vulnerable to deteriorating effects than men in most behavioral areas.

Deteriorating effects of therapy were more noticeable in individuals having greater sclerosis. Although deterioration occurred, it did not reach practical significance. Therefore, there appears to be no reason for withholding electroconvulsive therapy as a trial procedure in cases in which the causal factors in an illness are mixed or obscure and in which the treatment course is limited to six or less given at twice-weekly intervals.

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RESERPINE, in doses of 0.5 to 6.0 mg. daily, causes patients to become less agitated, disturbed, and demanding, and more cooperative. Confusion, disorientation, loss of memory, and other signs of organic involvement do not appear to be greatly affected, nor does the course of depressions appear to be altered. In some patients, the lethargy produced is a deterrent to further use after a few weeks.

Newly admitted alcoholic patients show reduction and sometimes elimination of restlessness, apprehension, and tremors, and nausea and vomiting on 200 to 400 mg. daily of chlorpromazine (Thorazine). Confusion, disorientation, and memory loss are not dramatically affected by the drug.

Chlorpromazine was administered to 10 male geriatric patients, starting with a 50-mg. dose, which was increased gradually to 400 mg. daily. Five of the patients over 60 died within six weeks after starting the drug, but there was no evidence that chlorpromazine was directly a cause of death. Conclusions drawn at the hospital from analysis of each patient's death were that chlorpromazine lessened the manifestations of and masked the existence of concurrent illnesses leading to delay in treatment until the patient entered an irreversible terminal state.

E. F. GALIONI: Reserpine and chlorpromazine. Their use in alcoholic and geriatric patients. California Med. 85: 97-99, 1956.

Impressions of Mexico

Report on the Pan American gerontologic congress

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◆ Having just returned from nine days in Mexico, my still vivid impressions may be of interest to you. The First Pan American Congress on Gerontology, held in Mexico City from September 15 through September 22, constituted an excuse for the trip.

I do not want to elaborate upon the scientific and sociologic value of international congresses in general or of this one in particular. However, this Congress was so typical of most international meetings that a few comments may be pertinent.

Immense enthusiasm is required to plan, organize, and carry through with any such international affair as a scientific congress. Also requisite are skill and judgment. The promoters and directors of this First Pan American Congress on Gerontology deserve the highest mark in enthusiasm and hospitality; in grading organizing skill and judgment there is room for criticism. As is so often the case, the enthusiasm of the program planners outstripped their judgment; there were too many papers and no opportunity for discussion. Many of the papers presented were but restatements of material previously published. Thus there was far more gravy than meat in most of the sessions. The papers presented in English, given largely by gerontologists of the United States and Canada with a few representatives from Great Britain, contained material which was not new. One knew in advance what was going to be said, even without having followed the literature, for the proceedings containing abstracts of the talks were published in advance and were readily available. I feel that to offer but restatements of work previously published is an insult to those who attend the Congress. Serious students of gerontology and geriatric medicine follow the international literature and should be aware of what has been going on. Furthermore, the running translation into English of speeches given in Spanish was sadly inadequate. The system of individual earphones worked very well, but what one heard was a sigh, and "Ah, it is too bad, but this is too technical. I cannot translate." This was followed by a long pause and then perhaps three or four words here and there, wholly unrelated to what preceded or followed. Apparently translation from English into Spanish was much more effective for the attentiveness of the audiences was truly surprising.

How much better it would have been if the printed abstracts or mimeographed copies of the papers had been circulated and the sessions devoted to discussion. A meeting of minds, rather than repetition of already recorded researches, would have been far more instructive. One gained much valuable information, stimulation, and inspiration from informal

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conversations between sessions, at lunch, and in the lobbies.

There was considerable unnecessary confusion. For example, advance programs sent to those who registered by mail stated that one could and should register at a stated hotel on Saturday the fifteenth at any time from 9:00 until 5:00. On attempting to do so at 12:45 I found the registration desk all set up, but wholly deserted. A bell-hop informed me that those in charge should be back after 3:00 and their siesta. No sign; no forewarning. A wholly unnecessary trip across the city is hardly helpful in building esteem for organization. Secondly, the program announced a social cocktail hour as an opportunity to meet representatives from the many different countries, naming a restaurant that does not exist! Only an hour or so before this gathering was the registration desk informed where it would be held.

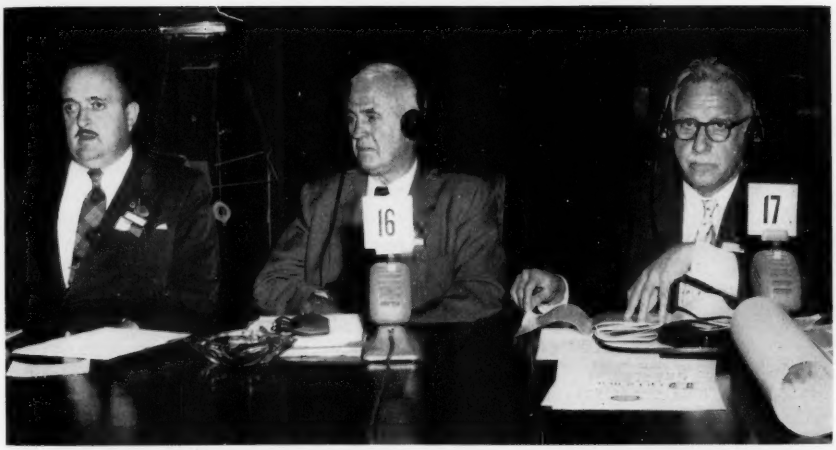
It is true that these are minor matters, but for a stranger having some difficulty with a foreign language they can be annoying.

The Setting for the Congress

The sessions were held on the magnificent new campus of the University of Mexico. The University has been built as a separate suburb of Mexico City. It is a show place. The huge buildings are extremely modern; the campus spreads out over many, many acres, with magnificent fountains and immense murals created in brilliantly colored mosaic. Unfortunately, however, these vast stone murals are, in most instances, merely put into a wall of a building with no more relationship to the architectural structure of the building than a billboard. Some of us felt that the University campus was produced as a stage set, perhaps designed by some Madison Avenue advertising agency, just for show. We learned that so much money had been spent on the buildings and grounds that funds available for a faculty are inadequate. Herein the Mexicans are not original, for such a state is sadly typical of too many of our own educational and governmental institutions. Many a university campus, and the Mall and Constitution Avenue in Washington cause me to ponder over the money spent for gray stone and wonder whether there is anything left for gray matter.

There was more politicking than science. Several so-called "plenary sessions" were devoted to persuading this international assemblage of scientists, and sociologists to approve a previously drafted model law pertaining to the welfare of the aged which the Mexican organizers hoped to present to the Mexican Legislature. Such political maneuvering was, to my mind, an abuse of the function of the Congress although it received hearty cooperation from certain North Americans.

I had deliberately attempted to avoid being on the program so that, for once, I might concentrate upon listening, but on this occasion the President of the Congress, Dr. Manuel Payno, insisted I sit with the officers and dignitaries and make a few remarks. Though I deeply appreciated the honor done me, alarm over the clearly apparent use of the Congress for political purposes made me feel obligated to speak frankly. After expressing appreciation for the beautiful wording of the model law and its highly altruistic intent, I expressed profound regret that it completely omitted two of the most important facets of need. In the first place, it made no mention whatsoever of education so that by anticipation and prevention premature disability might be avoided. All emphasis was upon rehabilitation after disablement. In the second place, the document omitted the slightest mention of an individual's own responsibility for self. Under these circumstances I felt that approval of the present material or document was premature and unwise. Obviously, these comments were unwelcome. Such was



At the plenary session: Left to right—Dr. Manuel Payno, president of the Congress; Dr. E. V. Cowdry, chairman of American Committee on Cooperation; and Dr. E. J. Stieglitz.

made clear at the time. Nevertheless, I still think they are valid.

The American Tourist

The Mexicans excelled in being magnificently generous hosts. They provided a variety of extraordinarily interesting entertainment for the members of the Congress. In contrast, there were several from the United States who were anything but magnificent guests. The usual American tourist is obnoxious enough; we had reason to be ashamed of the behavior of some professional colleagues who should have known better. One evening, when the Congress had arranged a most beautiful program of Mexican, Indian, and Spanish dancing with magnificently colored costumes, and had arranged to have special buses to take us back to our hotels, a small nucleus of doctors from the United States broke into loud, ribald, silly, and sophomoric song in the back of the bus. Had they been able to sing it would still have been in poor taste, but they produced mere noise like a group of inebriated alumni back on Homecoming day. The disgust of the Central and South American physicians and scientists and their wives was obvious.

The Mexican People

To me the most significant experience lay in the opportunity to see, study, and sense the personality of the Mexican people. Though time was short, by avoiding official tours and the tourist hotels, and mixing as unobtrusively as possible with the people, both big and little, a physician trained to observe can learn much quickly. The Mexicans fascinated me. They were not what the "popular" concept makes them out to be. Indolence was nowhere detectable; poverty was extreme in many areas but it was invariably associated with dignity, stoic composure, and an intrinsically humble pride wholly lacking in arrogance. There was no fawning or descent from dignity at any time. Yet stiffness did not chill the dignity for it was always friendly. Despite the obvious poverty there was no begging; only offers to sell something. And these were never obtrusive or offensive; a shake of the head was sufficient denial. Despite an intense congestion of milling crowds on

the sidewalks (narrowed by street vendors selling everything from sandals, shoeshines, straw hats, belts, cheap jewelry, and toys spread upon the curb, and 6 to 15 sellers of tickets for the national lottery to the city block) there was no pushing or jostling. Jaywalking was universal and yet the heavy traffic flowed rapidly. The traffic police—a separate force—displayed conspicuous efficiency in avoiding snarls; their directions were obeyed promptly and scrupulously. Courtesy is so uniformly universal it is clearly sincere.

It was notable that many of the sellers of lottery tickets wearing official caps with the letter "L. N." thereon, were blind. Apparently, instead of charity in the form of a dole, the state employs these blind men and women. It is to the credit of the Mexican people that this can be so, for almost all transactions are with paper money and cheating the blind would be easy. Their numbers in this occupation attest the honesty of the Mexican public far more eloquently than anything else could.

The City and the Markets

Mexico City is an extraordinary community. It has grown with remarkable rapidity in the last few years to a present population of over 4,000,000 souls. It reveals the extremes of antiquity and vigorous modernity. The very old, dating from Spain's conquest of Mexico, is immediately adjacent to the extremely modern. New buildings are everywhere under construction—most of them large, often offensively modern, and constructed of reinforced concrete with exterior walls consisting almost solely of glass. For example, I chose to stay at a small, downtown hotel which does not attract tourists. Directly across the narrow street is a building built about 400 years ago (1550) whose outer stone walls are largely covered with beautiful blue and white tile. Immediately next to the hotel is rising a skyscraper, about 30 stories high, exterior all glass, with spun aluminum window frames and glass and aluminum doors and entrances. Across the square is the all white marble Palace of the Fine Arts, reminiscent of Italy, Spain, or Paris. Alongside many other new and very modern office buildings, hotels, government buildings, shops, and apartments are structures from one to four hundred years old. The open market areas, where the poor Mexicans and Indians shop, may abut upon some magnificent plaza, cathedral square, or palace.

These markets are fascinating. One can buy almost anything there: beautiful hand woven material is available "for a song" even if one is not in the best of voice. In these markets one sees the backbone of Mexico—the basic population of peasants, largely Indian in origin, lean, stolid, hard-working, frugal, patient, and always friendly. Their children, though often ill-clothed, were rarely ill-nourished and seemed surprisingly happy and contented. There was nowhere evident the greed, petulant restlessness, and "Gimme" this or that so typical of many children north of the border. Perhaps this is due in part to very close family relationships and the continuous intimacy which small babies have with their mothers. Small babies are carried inside the rebozos, or large shawls which these women wear. The babies nestle inside this garment, usually slung to the left side of the mother's breast. I was given to understand that the little ones are often permitted to nurse in peace while the mothers go on about their business of barter and exchange in the open markets. This intimate closeness of mother and child may be a fundamental reason for the clearly discernible equanimity, sense of worth, and dignity of the Mexican people. It is only among the politically minded that one becomes aware of intense ambitions, a sense of urgency in demonstrating self-importance.

September 16 was the Mexican Independence Day, corresponding to our Fourth of July. On Saturday night, the fifteenth, the streets were filled with people. The noise of many firecrackers, singing, and dancing, interspersed with the wail of ambulance sirens continued until the stroke of midnight. Then it became suddenly silent, for 98 per cent of the people are devout Catholics and the explosion of firecrackers on a Sunday would be an abomination in their eyes. On Sunday morning, a military parade lasting four hours brought hordes of spectators who were far more interesting than the cavalcade of army cars, motorcycles, and tanks.

Later, on Sunday afternoon, at the weekly bullfight, observing the immense crowd was as interesting as what went on in the ring. These people appreciate finesse. They appreciate courage and gallantry and the long established ritualized customs of the bullring. They come there to see, not the slaughter of the bull, but the exposition of an art which involves many highly complicated, formalized procedures. They were quick to criticize; sloppiness was condemned; especial grace, ability and skill, and particularly skill associated with personal courage, were appreciated and applauded. The enjoyment of a bullfight is an acquired taste. I, naturally, was unable to acquire this in full in just one afternoon, but I could sense the significance of the performance. However, on leaving we met two or three American gerontologists whose reactions were quite different. One commented: "I think they do this better in the Chicago stockyards." The other said: "How crude!" Neither had been sensitive to the finesse of the combat.

The Creative Arts

Again and again I was impressed with the vigor, originality, and variety of modern Mexican architecture, music, painting, and other creative arts. I became convinced that in Mexico a creative person with a new concept was as a rule far more concerned with attempting to develop that concept in what to him was its purest form, rather than whether it would be acceptable to others. Their colors and designs are vivid, vigorous, virile, and sometimes startling. Not all are what we would call beautiful, but many have extraordinary beauty and originality. They seem to grow in significance with contemplative observation. Contrasting the Mexican and North American forms of artistic expression led me to feel that creators of the new in art and music in the United States were less sincere in that there was concern that their creative work be acceptable and salable. Idolatry of the almighty dollor and a need for reassurance by acceptance by the herd does not, as yet, dilute or prostitute Mexican creativity as they do here in the United States. The conviction fitted my impression that a fundamental type of mature courage is more frequent in Mexico and confirms my sad and regrettable opinion that individual courage and maturation are depreciating in the United States.

An all day trip into the countryside revealed the physical beauty of this high land. Mexico City itself is some 7,400 feet above sea level. It lies in a valley surrounded by mountains. Crossing these mountains to small towns beyond the rim reveals the ruggedness of the mountain country and accounts for the poverty of the countryside. Mexico's agriculture is profitable on the southern sea coast, not here in the mountains.

It is clear that I've fallen in love with Mexico and her people. There is much we can learn from them if we are able to silence our own conceit and arrogant pride in the material and realize that to know why is as important as to know how. I wish I could have stayed much longer. Residence there, combined with sincere study, would profit many of us.

Response potentials of vascular tissues and the genesis of arteriosclerosis—a review

Part II C. Hemodynamic factors

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◆ The mechanical theory of the genesis of arteriosclerosis holds that the vascular changes characteristic of this disease are the end result of general and local hemodynamic factors acting for a long period of time. The arteriosclerotic lesion has thus been considered by some as representing the end result of reparative processes to wear and tear effects produced by such forces, and by others as a compensatory or adaptive phenomenon which serves to maintain the lumen diameter and thus a relative constancy of the mechanics of blood flow.

The mechanical theory probably had its origin with Cruveilhier, who, although he looked upon arteriosclerosis as fundamentally an inflammatory process, nevertheless made the interesting observation that the calcareous deposits constituted a protective mechanism against overdilatation.[1] Virchow,[2] who also looked upon arteriosclerosis as an irritative phenomenon in which an inhibition of material from the passing blood stream called forth an almost neoplastic proliferation of the connective tissue of the intima, considered mechanical factors of the greatest moment. He believed that lesions developed in regions where the force of the blood stream was straight, and tearing and stretching of the intimal coat might occur. Klotz stressed the irritative effects of infectious or toxic factors, but also recognized the importance of regional strain.[3] He pointed out the preponderance of sclerosis in the lower extremities of people much on their feet, and demonstrated the experimental reversal of this localization in animals suspended for long periods with head down.

Thoma first offered a detailed account of arteriosclerosis as a compensatory phenomenon to the wear and tear effects of hemodynamic factors.[4] According to his view, various disturbances in nutrition as well as the deterioration of old age leads to a weakening and loss of resiliency, resulting in a bulging of the arterial wall under the influence of blood pressure. He considered the resulting dilatation as rendering the artery too wide for the needs of the part supplied; and, just as the umbilical arteries close as their function ceases, so other arteries develop a thickening of the intima to adapt the caliber of the vessel to the needs of the organ which it supplies. According to this view, with progressive deterioration of the media, the demand for intimal thickening continues and the nutrition of the thickened intima is further impaired, resulting in the formation of a hyaline fibrotic atheromatous and calcified lesion.

Still others believed that various stresses were the primary causes of degenerative and regenerative processes in elastic tissue, and that the latter were followed by retrogressive changes, especially fatty degeneration.[5,6] Such effects

on elastic fibers have been the subject of recent reports by Policard[7] and by the author and coworkers.[8-14]

Proponents of the lipid-metabolic thesis either regard hemodynamic factors as of secondary importance in that they may influence localization of lesions,[15] or consider their effects as unrelated to intimal plaque formation. They contend that aging changes show a linear relationship with time, whereas the incidence of arteriosclerosis, after an earlier rise, remains at a fairly constant level after the sixth decade.[16] Our initial report on this subject contains a graph clearly refuting this, which shows that medial calcification of the aorta attains an average maximum intensity in the age group 50 to 59, after which the curve remains flat. Aschoff says that "it is a well-known fact that there are persons with more or less worn-out cardiovascular systems who live to a ripe old age."[17] Lansing believes that the mural aging changes and lipid deposition are two temporally and quantitatively distinct reactions.[18] Finally, some of the degenerative changes of the media, particularly beneath plaques, are considered as a secondary pressure phenomenon, although recent observations that early and constant medial thinning occurs in the aorta and iliac arteries indicate that this is not a secondary result of the atheromatous process, but an essential part of it.[19]

In a negative sense, the failure of the lipid-metabolic theory to explain the distribution of arteriosclerotic lesions makes necessary the continuation of a search for other causes. In a more positive way, mechanical factors and vascular responses are not uniform throughout the body and it appears that a correlation can be developed between such factors and responses on the one hand, and the localization of intimal plaques on the other. The peculiar susceptibilities of certain vessels, such as the aorta, coronary and cerebral arteries, and those of the lower extremities, to such complications as thrombosis, aneurysm formation, and rupture, require a more adequate explanation than is being offered by the proponents of the lipid-metabolic thesis.

This section has for its primary purpose the presentation of observations supporting a causal relationship between vascular responses to hemodynamic factors and formation of intimal plaques. Since a time factor enters into a consideration of hemodynamic factors, it may be well to clarify the meaning of the term "aging." As we have used it in connection with the arteriosclerotic process, "aging" connotes changes which are largely attributable to "wear and tear" effects of hemodynamic forces. The less intense the hemodynamic forces, the longer will be the period required for development of vascular lesions.

It should be constantly emphasized that arteriosclerosis is a disseminated disease involving the total wall of many arteries according to a specific pattern. A somewhat superficial expression of these facts is gleaned from the conventional classification of arteriosclerosis as atheromatosis of elastic arteries and their major branches, Mönckeberg's sclerosis of larger muscular arteries, sometimes with superimposed atheromatosis, and hyperplastic or hyalinizing arteriosclerosis of small muscular arteries and arterioles along with hyalinization of capillaries, particularly in hypertensive persons. Atheroma formation is not a characteristic of these terminal units of the arterial side of the circulation. Even such a superficial classification implies that certain common etiologic factors may be responsible for these varied features of the arteriosclerotic process, since it is generally recognized that all are intensified in hypertensive individuals. Generally overlooked, however, is that the differences in various vascular segments may be attributed to their tissue re-

sponse potentials, based on their initial histologic characteristics, as pointed out in part I of this review.

In this section, then, we shall present a discussion of general and local hemodynamic factors which are responsible for calling forth tissue responses in blood vessels and show how such responses lead to the arteriosclerotic lesions characteristic of the various groups of arteries.

Blood Pressure

Several authors have emphasized the effects of blood pressure, based on the recognition of an increased intensity of the arteriosclerotic process in individuals with hypertension.[20,21,15] Moschcowitz believes that blood pressure is the most important factor in the pathogenesis of arteriosclerosis and stresses particularly the diastolic level.[22] He has expressed the role of this factor in the equation,

Arteriosclerosis=Intravascular Tension+Time

in which is recognized the fact that even normal intravascular tension acting for a sufficiently long period may produce arteriosclerosis. When the intravascular pressure is maintained above normal levels, the time required for lesions to appear is reduced.

He points out that segments of the circulation which operate at low tensions are normally relatively immune to the arteriosclerotic process unless conditions operate to increase intravascular pressure. Significant arteriosclerosis develops in the pulmonary arterial circuit only under conditions of hypertension. However, it should be pointed out that factors which produce hypertension of the greater circulation generally spare the pulmonary arterial system.[23,24]

In coarctation of the aorta, that portion proximal to the constriction has an elevated tension and develops severe sclerotic changes, while the part distal to the constriction operates at a low pressure and shows minimal or no sclerosis, which is opposite to the normal situation.

The veins in general operate at low tensions and are relatively immune to sclerotic processes. Yet when the pressure is pronounced, increased sclerotic processes occur, including formation of atheromatous plaques. This is the case in varicose veins and on the venous side of arteriovenous aneurysms.[25] It has been shown that sclerosis occurs in a segment of vein sutured between divided ends of the aorta.[26] Furthermore, phlebosclerotic changes have been noted in profound venous congestion.[27,28] Sclerosis of veins of the portal system is a common finding in hypertension of that system associated with cirrhosis of the liver, or proximal to obstructive lesions of the portal vein. A high frequency of venous atheromata has been observed in the region where the orifice of the left common iliac vein joins the inferior vena cava.[29] This is the area of maximal mechanical stress in the whole venous system. Here the alterations leading to atheroma formation are comparable to those in arteries, since the magnitude of mechanical strain is also comparable.

Winternitz points out that the tensile strength of the vessel wall is determined by the tough, inelastic adventitia rather than by the more delicate and distensible media and intima.[30] According to his theory, when pressure within the lumen is increased, the intima and media become compressed between this force and the outer coat, with concomitant compression of the intramural capillary bed. This impairment of the intramural vascular supply would then lead to degenerative changes in the artery wall.

Hydrostatic Tension

These considerations, however, do not explain the peculiar susceptibility of certain areas to wear and tear. In large part, this may be accounted for by a concept which relates hydrostatic tension to vascular responses. Tension in any par-

TABLE 1

EFFECTIVE TENSION COMPARED WITH INTENSITY OF ADAPTIVE STRUCTURAL CHANGES

Vessel	*Mean pressure (systolic)*	*Radius*	*Tension (dynes/cm.²)*	*Elastic tissue*	*Plaque formation*	*Calcification*
Group I						
Aorta	100 mm. Hg	1.3 cm.	170,000	4+*	4+*	4+*
Pulmonary artery	40 mm. Hg	1.5 cm.	78,000	4+	0.5+	0.5+
Group II						
Large arteries	100 mm. Hg	0.15 cm.	20,000			
Coronary				1.5+	3+	3 +
Splenic				1.5+	2+	2.5+
Hepatic				1.5+	2+	2.5+
Renal				1.5+	2+	2.5+
Basilar				1.0+	3+	2.0+
Group III						
1st order branch	70 mm. Hg	0.05 cm.	4,550	0.5+	1 +	1.0+
2nd order branch	65 mm. Hg	0.03 cm.	2,550	0.5+	0.5+	0.5+
3rd order branch	65 mm. Hg	0.02 cm.	1,700	0.5+	trace	trace
Arteriole	60 mm. Hg	0.015 cm.	1,170	trace	trace	trace
Capillary	30 mm. Hg	0.004 cm.	16	none	none	none

*Aorta has been arbitrarily selected as standard with which to compare other arteries. Mean pressure and radius used for calculation of tension were obtained from Glasier, Medical Physics, Vol. 2.

ticular vessel is an expression of the stretching force excited by the hydrostatic pressure on the vessel wall.[31] This force in turn is counteracted by the vessel wall. According to Burton blood vessels can be considered as cylinders open at both ends and filled with fluid, whose hydrostatic pressure is greater than that existing outside the vessel walls.[32] The hydrostatic pressure acts at right angles to the wall, tending to distend the vessel and increase its diameter. This force is opposed by the tension developed in the wall, tending to diminish the diameter of the vessel. This tension consists of three main components:

1. Elastic tension caused by stretch of the vessel wall and the elastic fibers. This is determined by the ability of the elastic fibers to recoil after such stretching.
2. Active tension caused by contraction of the smooth muscle elements in the wall. This is a function of the vasomotor tone regulated by nerve impulses, of certain pressor or dilator substances in the blood stream, and of certain hormones, particularly norepinephrine.
3. Interfacial tension caused by possible surface tension between the fluid in the vessel and the inner surface of the wall, which will be present unless the wall is completely wettable by the fluid.

Burton has shown that the hydrostatic tension in any particular vessel may be calculated by applying the classical law of Laplace, represented by the equation $T = P \times R$: in which P is the excess of the hydrostatic pressure inside the vessel over the local surrounding tissue pressure in dynes/cm.²; T, the tension developed in the wall in dynes per centimeter; and R, the radius of the cylinder.[32]

In table 1 we have calculated the hydrostatic tension generally obtaining in various segments of the circulation in normotensive subjects and have related this to the quantities of elastic tissue in each segment and to various degenerative phenomena associated with the arteriosclerotic process. With the exception of the main pulmonary artery, intimal plaque formation and calcification of the vessel wall, particularly of elastic fiber, appear directly correlated with the operating hydrostatic tension. It is apparent from this data that the radius

of the vessel is more important than the blood pressure, since the latter changes only by a factor of about 4 between the aorta and the capillary bed, whereas the radius changes by a factor of 325. The radius therefore appears most important in determining the magnitude of the total maintenance tension requirement on the wall to prevent its permanent dilatation. Nevertheless, the blood pressure may assume greater importance when a state of hypertension exists.

Willis points out that the "elastic tension is the most efficient way of providing maintenance tension to hold the wall of the vessel against the prevailing hydrostatic pressure of the blood without any continuous expenditure of energy."[31] Thus the quantity of elastic tissue in any particular artery appears to be related to its normal tension requirement, and one wonders if the latter may already act as a determinant in embryonal development influencing the initial structure of a particular artery. Although no proof of such a concept exists, there are certain suggestive observations. Thayer and Fabyan have reported splitting of the internal elastic lamella in the radial artery beginning with the seventh month,[33] and Jackson's studies on the histogenesis of the aorta show a splitting of the internal elastica at the 120-mm. stage in man.[34] Three types of "splitting, knotting and fraying" in cerebral arteries have been observed at eight months post partum, and local patches of fibroelastic thickening in the aorta have been observed at six weeks post partum.

The fundamental Laplace equation is applicable to straight arteries, but Willis has modified it to also take into account curved vessels and has shown that the hydrostatic tension is highest along the inner curve of a vessel and so is the intensity of the arteriosclerotic process.[31] The exception to this generalization appears to be the arch of the aorta, where the modified formula may not apply because of the origins of the roots of the great vessels. If this view is correct, then the development of tortuosity of arteries associated with the arteriosclerotic process would tend to intensify the latter.

The predilection of plaque formation for sites of branching of arteries can also be explained by an application of the Laplace equation. At the origins of many branches there is an "Indian-Club" type of dilatation, thus providing a larger radius than more distal portions of the branch.[37,38] Furthermore, there is a normal progressive dilatation which always occurs at the approach to a major bifurcation corresponding to the site of intensified plaque formation.[31] In addition, at the point of origin of a branch the hydrostatic pressure is that of the parent trunk and the tension requirement would likewise be that of the latter. However, the structural characteristics, particularly in hybrid arteries, are those of the branch, and, in general, there is a progressive diminution either in quantity or in thickness of elastic fibers as artery branches diminish in caliber; this therefore results in a loss of efficiency in the development of intramural tension.

Neither Burton nor Willis has thus far taken into account that arteries operate not under a constant but a pulsating pressure created by the ventricular pump.[32,31] Wiggers has defined the vascular pulse resulting from such cardiac action as the expansion of the vessel which the pressure pulse produced in any part of the arterial system.[38] Under normal conditions the pressure pulse in the aorta and some of its major branches show an initial steep rise from the rather large volume of blood suddenly ejected by the left ventricle. This volume is only partially moved along; a very considerable portion of it is stored by the expansion of the aorta and then slowly advanced as the latter contracts. More distal arteries show a different pressure pulse curve than the aorta. In the radial artery, the pressure pulse rises less

abruptly to a peak and the systolic pressure at this point does not deviate greatly from that in the aorta. In the femoral artery, however, the rise in pressure pulse is much more abrupt than in the radial and the systolic pressure reached actually exceeds that of the aorta, often by as much as 20 or 30 mm. Hg.

If this principle applies equally to other peripheral, muscular arteries, then the mean systolic pressure gradients shown in table 1 are subject to modification, and, at least in some instances, the actual maximum intramural tension requirement may be higher than shown. That such modification may be of significant magnitude is indicated by Wiggers' observation that the pressure pulses recorded from more peripheral arteries, such as the dorsalis pedis, show even greater augmentation of the systolic pressure.[38] In detailing these variations in pressure pulses, Wiggers states that the aortic pressure exceeds the femoral pressure significantly during the early portion of systole, but a reverse pressure gradient temporarily supervenes during the latter part of systole, which actually results in a backflow of blood toward the aorta.

Furthermore, Bramwell and associates point out that when the artery wall loses its resiliency or when blood pressure is high, the pulse wave attains much higher values.[38] Thus, under the latter conditions, it would also be expected that backflow would be intensified.

Cardiac Thrust

The efficiency of the aorta as a compression chamber-buffer is directly dependent upon its resiliency. With the progressive loss in such resiliency which begins at a relatively early age, there is also a progressive loss in efficiency in the control of the outflow into those segments of the arterial system distal to the aorta. Wiggers points out that the "Indian club" enlargement at many bifurcations may serve in a similar capacity, but these are subject to the same intramural changes leading to elasticity loss. Progressive calcification of elastic elements in the wall leads to increasing rigidity, and, as a result, the direct thrust of the heart in systole is transmitted much farther to the periphery than with a normally elastic aorta and major branches. When blood is suddenly injected into the aorta, a positive centrifugal pressure wave is transmitted to all branches of the aorta. Its magnitude may be dependent upon the efficiency of the aorta as an elastic buffer, and its speed of transmission is such that it reaches the furthermost portions of the arterial tree before systole is over. At all points at which this wave meets increased resistance through rapid branching of arteries, there is gross rebound of the blood column and centripetal wavelets are reflected back at velocities dependent upon existing pressures. According to physical laws, such reflections occur with change of phase, indicating both open and closed states. Wiggers states that we may therefore anticipate reflection of small negative waves from such loci as the division of the carotid at the base of the skull, the bifurcation of the aorta and its branches, and reflections of large positive waves from numerous smaller divisions of the arterial tree.[40]

Again, it is apparent that such reflections and eddy currents occur at sites of special susceptibility to the formation of arteriosclerotic plaques. Furthermore, if one takes into account the observations that the mean pulse wave velocity increases progressively with age, while the mean resiliency progressively diminishes,[39] it becomes apparent that the "wear and tear" effects on arteries may serve to intensify these phenomena. It is also apparent from these considerations that sites of bifurcation of arteries must, therefore, be foci of considerable churning of blood.

Vibration

Whenever tension is suddenly changed in the arterial system, free vibrations are set up. Conditions for such vibrations are most favorable in the immediate branches of the aortic arch during the beginning of ejection and upon closure of the semilunar valves. These vibrations are also transmitted to the immediate aortic branches; indeed they may even be somewhat intensified. They are gradually damped and transformed into small slower vibrations in the upper carotid artery and evidence for them is entirely lost in the radial pressure pulse curves. When the left ventricle ejects a large volume into a lax aorta, a second set of free vibrations is superimposed at the top of the initial steep rise in pressure pulse during injection. According to Straub, the natural frequency in the arteries of the arm lies between 3.6 and 4.8.[41]

The susceptibility to plaque formation of the immediate branches of the aorta, including the coronary arteries, suggests that such vibrations may also play a role in the deterioration of tissue elements in the wall, although experimental proof is lacking. Furthermore, it would be important to know what effects the increasing rigidity of the aorta would have upon the frequency of such vibrations and on the distance of their transmission. It is also conceivable that they may play some role in the development of eddy currents at sites of bifurcation.

Volume Flow

Volume flow may change with alterations in cardiac output, but it may also change as a result of local hemodynamic factors. The more peripheral arteries, by contraction of muscular elements, can reduce the lumen appreciably. They may do so as an adaptive phenomenon to variations in volume of circulating blood. Thus, if an arterial cylinder is suddenly distended by increasing the internal pressure, the vessel contracts and, under static conditions, an increase in pressure occurs. Such a state probably exists when the aorta, which normally stores nearly half of the blood discharged by the left ventricle during systole, loses its distensibility through "wear and tear" effects on its tissues and comes more to resemble in function a simple delivery tube than a reservoir. A contraction in diameter may also occur when the internal pressure rises because of vasomotor action.

It is unlikely, however, that muscular arteries participate in propelling blood to the periphery, since it is difficult to conceive that contractions of nonstriated muscle can occur at frequencies equal to those of the heart beat. On the other hand, contractions of muscular arteries take place independently of those of their distribution arterioles and do not exhibit rhythmic variations.[42] Their contraction alters the resistance to stretch and this affects the character of pulsatile flow. These considerations appear to be particularly important as regards the pathogenesis of relatively acute degenerative changes leading to hyalinization and calcification of smooth muscle; these tissue alterations seem to occur particularly under the influence of norepinephrine when volume output of the heart per unit time is increased and "run off" through capillaries and arterioles diminished through constriction of the latter. Vessels which are in effect end-arteries and lack shunts, such as the splenic and renals, are particularly susceptible to these degenerative phenomena which seem to occur when there are opposing asynchronous conditions of distention and contraction. Those considerations are particularly important in relation to the sclerotic changes in small arteries, arterioles, and capillaries.

Gravitational Forces

Dock has pointed out that arteriosclerosis is more severe in the abdomi-

nal than in the thoracic aorta and attributes this to the higher blood pressure in the former segment.[43] A similar difference in blood pressure and intensity of arteriosclerosis exists between the bifurcation of the aorta and its arch, as well as between the arteries of the lower and upper extremities. Hemodynamic factors which explain such differences, at least in part, have already received consideration. An additional factor supplementing the pressure developed by the cardiovascular system may be the gravitational effect of the column of blood occasioned by the upright position in man. Such a conclusion appears to be validated by the observation of Klotz that the distribution of sclerotic patches in rabbits may be changed by varying the position of the animals.[3]

Viscosity and Friction

These two factors deserve mention, although there is little information available as to their importance. The viscosity factor is a tricky component to evaluate in the body and is entirely different from that predetermined in vitro.[38] This is in part due to effects that the small diameters of capillaries have on the rate of blood flow, and in part on the interchange of plasma which takes place in these small channels.

Viscosity probably does not appreciably change until the blood reaches small arteries, arterioles, and capillaries. The friction factor also increases as the caliber of vessels diminishes. While neither of these may play a significant role in degenerative changes in large arteries, they may be important in the genesis of degenerative and inflammatory phenomena in small arteries, arterioles, and capillaries which have been observed in experimental hypertension.

Shearing Forces

In 1915, Albutt proposed a shearing force resulting from a slip between intima and media during contraction and dilatation to account for the stimulus to intimal thickening.[44] However, Krafka has shown that, when the diameter of the lumen is doubled, the circumference of the intima also doubles, but the inner wall of the media at the same time increases 199 per cent, giving a shearing factor of only 0.5 per cent.[45] On the other hand, the shearing factor between the media and adventitia with doubling of the lumen is 3.8 per cent. This observation appears to support the opinion that tube wear and tear from shearing is more marked between the middle and outer third of the cylinder. Krafka discounts the importance of such a shearing force on the basis that it is unlikely that during life an elastic or muscular artery would dilate to twice its original diameter with pulsation; in the aorta, he estimates a variation between systole and diastole of about 15 per cent.[45]

Krafka's observations, however, assume a permissible degree of movement of layers of the artery wall which does not obtain in all cases. Other workers have pointed out that the intercostal arteries are more or less fixed to surrounding structures, close to their orifices from the aorta.[46,47,47] The aorta itself has only a loose attachment to the vertebral column from its origin to the fourth thoracic vertebra, but distal to this point there are distinct suspending bands which limit its movement. According to Duguid, these attachments produce a drag, leading to "splits and chinks" which tend to separate intima and media,[47] while Ranke believed that they effectively limited constriction of the aorta.[46] Willis points out that with each cardiac systole the aorta elongates besides becoming distended and there is tugging of the intercostal vessels which is released in diastole.[31] Wilens' experiments in rabbits, employing silver cuffs to envelop segments of the artery, indicate effects which such fixation may produce.[48] This investigator noted a tendency for atheroma to develop at the

junction of normal, unenclosed pulsatile arteries with the enclosed fixed segment. Harrison observed the localization of plaques at the edges of medial calcification which he had produced by feeding large amounts of vitamin D.[44]

While medial calcification may alter the degree of slippage between media and intima or media and adventitia by fixing the muscular coat, adventitial attachments would have the effect of altering movement between media and adventitia. The latter would constitute a shearing force on the vasa vasorum as they penetrate from the adventitia into the media and thus impair the intramural vascular supply. Since the intercostal arteries supply branches which form the vasa vasorum of the adjacent aorta, such effects would involve both the parent trunk as well as its branches.

Vascular Tissue Response to Hemodynamic Forces

It has been stated that "the atherosclerotic lesion is basically a local reaction of components of the vascular wall to influences which upset the balance between functional demand and the functional capacity of the vessel wall to fill the demand."[50] The foregoing considerations regarding hemodynamic factors indicate, however, that some of the latter obtain generally for all vessels, while others are predominantly local in their effects.

There seems to be general agreement that one of the universal effects of these hemodynamic forces in the vascular wall is a loss of resiliency, although, as we have pointed out, the relationship between this and intimal plaque formation remains in dispute. Such a loss of ability to rebound from distention, based on the simple observation of progressive dilatation and lengthening of the aorta, appears to have first been stressed by Wertheim,[51] Wundt,[52] and Polotebnow.[53] Kaufmann was probably the first to make extensive measurements and place such observations on a quantitative basis.[54] A number of earlier investigators employed strips of human aorta to measure elasticity curves.[55-68,45] Elasticity has been determined indirectly by measurement of the velocity of the pulse wave and application of Moen's formula.[69-72,65] In general, all agree that there is a progressive decrease in resiliency with age. According to some workers this is associated with a progressive increase in wall thickness, a diminution of elastic tissue and an increase in collagen fibers.[45,62,63,68] Krafka and Hass believe that this loss is not caused as much by an actual loss of elastic tissue as by an increase in connective tissue, which interferes with the function of elastic fibers.[45,63] The stimulus for such an increase in connective tissue, is a herniation of the intima through interstices and fenestrae between elastic elements caused by lateral pressures.[45]

The author and coworkers have shown that the curve of resiliency loss with age parallels closely the intensity of calcification of the media of the aorta,[8] and we have already remarked as to the effect which this increased rigidity has on the function of the latter as a buffer to variations in pressure and flow of blood and to the systolic thrust of the heart. We have also pointed out how such increased rigidity leads to intensification of turbulence of blood at sites of bifurcations of arteries.

As regards vascular tissue responses in the aorta under such conditions, histologists vary in their view as to the amount of muscle and its histomechanical arrangement in this vessel. According to Hürthle, one-third of the aortic wall is muscle,[73] but Benninghoff pictures muscle fibers as rather sparse and consisting of serrated, stellate rather than spindle-shaped cells such as exist in peripheral arteries.[74] Some believe that the contraction of muscle decreases the elasticity of the aorta,[75,76] while others hold that muscular contraction detenses elastic elements and so increases

aortic resiliency.[74-77] This difference of opinion results, in part, from differences in concept as to the sequence of muscle contraction in relation to elastic recoil. The superabundance of elastic fiber in the wall of the aorta tends to mask degenerative changes in muscle to the point that it becomes extremely difficult to determine to what extent calcification of the latter contributes to mineralization and rigidity of the wall.

Mineralization of vessel walls, while it does not contribute to active tension, may nevertheless prevent overdilatation and therefore serves to limit the increase in hydrostatic tension associated with vascular dilatation. It has been shown that normal young arteries contain only small amounts of calcium,[78-80] and we have observed that this is most intense along the endothelium. In later years, calcium is found chiefly in the elastic lamella, but is not generally found in muscular arteries except along the internal elastic membrane.[7] We have confirmed this observation as regards elastic tissue,[8-14] but have also shown that in the renal artery[11] and, to a lesser extent in some other muscular arteries, fibers of the external elastic lamellae, which makes the media elastic by penetrating inward, also calcify. We have also observed intensification of this process in hypertensive subjects. Furthermore, in certain arteries, such as the splenic, renal, and arteries of the lower extremities,[11,13] there are also deposits of calcium in and about muscular elements; these are similar to the mineral deposits observed in experimental animals following the injection of epinephrine.

Despite extensive investigations,[80-87,7] little is known of the significance of the affinity of calcium for elastic tissue. Nevertheless this affinity can be demonstrated in another way. In luetic aortitis, calcium may occur in foci of degeneration in intimal plaques, but the media, in which elastic elements have been largely destroyed, remains uncalcified even in aged specimens.[8]

In the most comprehensive picture of the mineral pattern in various arteries,[88] Ravault described a midzone mineral band in the media of the aorta which is more pronounced where branches arise, thus corresponding to the sites of most intense action of hemodynamic forces and most intense formation of atheromatous plaques. Of similar significance is his observation that mineral deposition in general is thicker in the angles of branching. In arteries which measure one to two centimeters in diameter, the band of calcification decreases in size and gradually disappears in smaller branches.

In some of our own studies, we were able to show that the intensity of calcification corresponds to sites of predilection for the formation of intimal plaques.[8-14] We further substantiated this observation in the aorta by direct chemical analysis of the calcium content of the wall in various locations.[12] We have also noted that such mineralization is not limited to the elastic elements originally present in the vessel wall, but that, as intimal formation progresses, newly formed elastic fibers and filaments appear and eventually show the same affinity for calcium as the original elastic elements. We concluded that it is such processes, rather than chemical reactions involving lipid deposits, which account for most of the calcification in intimal plaques. Our observations agree with those of Ravault in that, in Mönckeberg sclerosis, the most intense mineral deposits occur in and about elastic elements and to a lesser extent in and about degenerated muscle.[88] In some instances, the calcium appears to be incorporated within the elastic fiber, although, in most instances, it seems to be deposited only on the surface. The mineral deposits characteristic of Mönckeberg sclerosis are therefore not fundamentally different from those in other arteries; they differ only in degree.

While these alterations in the walls of arteries explain certain types of tissue responses to hemodynamic factors and the effects which they have of diminishing resiliency and at the same time increasing rigidity and limiting dilatation, they give no indication of a relationship to intimal plaque formation.

There are three distinct points of view in regard to intimal plaque formation. Some believe that these intramural changes which have been attributed to aging are distinct from and unrelated to intimal plaque formation.[78,89] Others are of the opinion that they may determine the localization of intimal lesions, but that the latter are fundamentally due to lipid-metabolic factors.[15] Still others believe that the intimal responses are due to hemodynamic forces.[80,4] From our own studies, it appears that the same hemodynamic forces which cause the medial changes are also responsible for the progressive thickening of the intima, and that the formation of intimal plaques represents a local accentuation of this basic process from the added effect of local hemodynamic factors.[13,14] Although it is not completely clear, it appears that the recently expressed views of Lansing fall somewhere in the first two of these viewpoints.[18]

Application of the principle of the Laplace equation, in particular, may not only account for vascular sclerosis as regards arteries generally, but also, in part, for susceptibilities of particular segments of the circulatory system. In general, it accounts for the diminishing intensity of the sclerotic process in any particular artery as it decreases in diameter. A most striking example of this is in the coronary arteries, which show the most intense sclerosis in their first few centimeters, with a gradual diminution in intensity distally, so that plaque formation becomes negligible in intramural branches. Although much has been made in the past of the high operating pressures of the coronary circulation,[31] the studies of Blache and Handler indicate that in the Negro, although hypertension is quite common, the intensity of coronary sclerosis lags almost a decade behind that in the white race and myocardial infarction occurs with considerably reduced frequency.[91] Furthermore, a recent report also indicates that hypertension is relatively unimportant in the pathogenesis of coronary arteriosclerosis.[92] Such observations point up the greater importance of radius in the determination of hydrostatic tension.

When one considers that such hypertensive producing substances as epinephrine do not produce peripheral vasoconstriction in coronary vessels, and that the coronary circulation fills mainly during the diastolic phase of the cardiac cycle, such observations deserve serious consideration. Furthermore, the Laplace equation takes into account the difference between intravascular pressure and that of the surrounding tissues. In the instances in which a portion of the anterior descending coronary artery lies buried in the myocardium, the buried segment is spared intense sclerosis, while branches of the same artery lying in the epicardial fat and therefore not surrounded by appreciable tissue pressure are affected by severe arteriosclerosis.[29] Vibration is another factor which may serve to intensify the arteriosclerotic process in the proximal portions of the coronary circulation.

The relation of intramural vascular tension to intimal plaque formation has perhaps not been as clearly proved in the coronary as in the cerebral circulation.[14] In the latter, we have compared the relation of internal diameter to wall thickness in various arteries of the circle of Willis before and after age 45. Despite thickening of the artery wall with advancing years, the vascular diameter increases. The increased thickening of the wall reflects the various collagenous and elastic tissue responses which on histologic examination prove to be primari-

ly intimal; these have been interpreted as indicating a response which serves to maintain a relatively constant internal diameter and thus also hydrostatic pressure. This mechanism is, however, an imperfect one, and the degree to which the vessel dilated reflects its inability to maintain the required intramural tension with advancing age.

Incidence of plaque formation is, again, highest in those arteries with larger lumina and highest hydrostatic tensions. The one possible exception is the internal carotid artery, which shows a somewhat lower degree of thickening and frequency of plaque formation than the basilar or middle cerebral arteries. While this difference may not be significant, it has been pointed out that the internal carotid artery may contain a sphincter which not only protects the distal segment of that artery, but also that portion of the circle of Willis which directly receives carotid blood. The protective factor of surrounding tissue pressure also obtains in the carotid artery because of the carotid canal in the base of the skull in which it travels. This artery is very rarely affected by severe arteriosclerosis, while the portions lying proximal and distal are notoriously prone to extensive involvement.[92,93]

We have also shown that, in the lower extremity, the frequency of plaque formation appears to be directly related to the operating hydrostatic tension, as is also the intensity of elastification and calcification as determined by microincineration.[13] However, the frequency of thrombosis is higher in the tibial arteries and in the dorsalis pedis than in the popliteal, presumably because atheroma formation in the former vessels of smaller diameter produces a more critical narrowing of the lumen and thus a more effective slowing of the blood stream. Willis believes that the protective influence of surrounding tissue pressure also applies here to a 2- to 3-cm. segment of the femoral artery lying in relation to the ilioinguinal ligament.[31]

Regarding the arteries of the lower extremities, the spectacular manifestations of so-called Mönckeberg sclerosis are generally recognized, but frequency and severity of intimal plaque formation appear to come as a surprise to many investigators. Rodda, who found intimal plaque formation quite common in this area, states that frequency and severity of these changes are comparable to that observed in the coronary arteries.[94] The intervention of thrombotic episodes may also be as common, but may be subclinical because of the existence of a much more adequate collateral circulation than in the heart.

Such observations lead us to conclude that hydrostatic tension stimulates the generalized progressive thickening common to many arteries, and that the degree of such thickening is related to degree of tension. Certain other hemodynamic factors operate to intensify such factors in local areas and lead to intensified thickening of the wall, including the intima; such reactions then proceed to development of intimal plaques. The latter are thus foci in which intimal proliferation proceeds at a more rapid rate. Even if lipids were not present in these plaques, narrowing of the lumen would proceed to thrombosis and loss of elasticity, to rupture or aneurysm formation.

As we have pointed out, there is a tendency at the present time to assume that lipids can gain entrance only, or at least primarily, from the blood stream. Winternitz presented observations showing that the organization of intramural hemorrhages may lead to release of lipid substances.[30] While most reports on intimal hemorrhages have dealt with the aorta or coronary arteries, Wartman has now observed this phenomenon in the pulmonary, cerebral, renal, iliac, and femoral arteries, noting that it occurs only in primarily diseased vessels.[95] Wells

stated many years ago that wherever necrosis occurs there may also be a release of fatty substances.[96] More recent observations show that lipids are also released in the processes of hyalinization of smooth muscle and such muscle fibers appear in many areas of intimal proliferation and subsequently hyalinize.[97] On the other hand, certain workers believe that hyalinization represents the end stage of a deposit of hematogenous origin (fibrin) on the endothelium of the vessel.[98,99]

Taking into account the various turbulence factors at sites of branching of arteries, it becomes apparent that such processes may also contribute to fibrin deposition and subsequent hyalinization and release of lipids, although it is not necessary to assume that this is the sole mechanism. Dilatation and loss of resiliency may also set up conditions favorable to fibrin deposition and incorporation of such deposits into the intima. This is an entirely different mechanism than that postulated by the adherents of the lipid-metabolic thesis and does not require an elevation of circulating lipids to account for the appearance of the latter in plaques. Our observations on intraparenchymal arteries indicate that intimal plaque formation may develop both from tissue responses of components present in the wall as well as by fibrin deposition on the endothelial surface.

Finally, the possibility exists that lipids may be released as a product of degenerative changes in elastic fiber. While this thesis remains to be proved, it appears to be supported by the older observation of Wells that yellow plaque-like lesions also appear in elastic-containing tissues other than arteries, such as ligaments, tendons, and joint capsules.[96]

Conclusions

It is apparent that the term arteriosclerosis, as used in this presentation, encompasses the reaction of the total artery wall as represented by its components. It is also apparent that many agents may produce this lesion; some of these act locally, others act on many vessels more or less simultaneously.

We prefer the term arteriosclerosis to atherosclerosis because of the broad connotation of the former and believe that the restrictive sense of the latter does not warrant the broad usage which it has received. Atherosclerosis overemphasizes the importance of the lipids in the lesion almost to the exclusion of the other tissue elements. It further overemphasizes the role of lipid metabolic factors in the genesis of common arteriosclerosis, again to the exclusion of other causal agents which may play at least an equal if not a greater role in this disease.

Arteriosclerosis may be segmented in the sense that it may involve a part or all of the vessels of an organ, or a particular segment of the arterial circulation, or it may be general. The segmental form is usually on an inflammatory basis, while the generalized or disseminated form may be either on a lipid-metabolic or hemodynamic basis. The latter two are distinguishable, at least in certain intermediate stages, in that the lesions in the lipid-metabolic disease are essentially the same in all vessels regardless of the organ in which they are located or their size, while those caused by hemodynamic factors have a characteristic appearance dependent upon location and size. Furthermore, there are no particular areas of "immunity" in arteriosclerosis resulting from lipid-metabolic abnormalities, whereas there is a characteristic pattern in the intensity and frequency of lesions in the hemodynamic form.

Particularly significant in development of complications is the fact that despite the excellent reproduction of the lipid-metabolic form of arteriosclerosis in experimental animals, there has been an almost uniform failure to reproduce these complications. On the other hand, it should be stated, in all fairness, that attempts to reproduce the hemodynamic

form of the disease in the experimental animal have met with only limited success. Nevertheless, any of the forms of arteriosclerosis, whether segmental as in the inflammatory disease, generalized as in the lipid-metabolic type, or disseminated as in the hemodynamic form, may lead to such complications; and, when the organ whose blood supply is thus impaired is a vital one, the result may be fatal. Present-day vital statistics are thus inadequate in that they do not indicate the nature of the underlying disease process.

It must be apparent to all who have extensively studied human autopsy material that by far the most common form of arteriosclerosis is the disseminated disease caused by hemodynamic factors. We have dealt with some of these factors, but considerably more work must be done before all of the important factors are clearly defined and the reactions to them recognized.

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SOCIOMEDICAL PROGRESS

Retirement attitudes of compulsory and noncompulsory retired workers

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Workers retired under a policy of compulsory retirement are as resistant to the new status as workers retired under a policy of noncompulsory retirement. However, in the compulsory group, resistance stems from fitness to continue working, while in the noncompulsory group, resistance stems from inability to continue working because of ill health or age.

◆ Studies of retirement attitudes suggest that workers are reluctant to retire.[1-6] The reasons for this attitude probably stem from a combination of economic, cultural, psychologic, and social factors. Presumably, workers required to retire at a specified age should be more resistant to retirement than those not so required, for there is a greater likelihood that they will be physically able to continue working. The purpose of this study is to compare two groups of retired workers, one leaving work under a policy of compulsory retirement, the other under a policy of noncompulsory retirement. The comparison between the two groups will involve attitudes toward retirement, reasons for these attitudes, self-reports of some aspects of job performance, and plans for and the utilization of added leisure time in the retirement period.

Material and Methods

The compulsory retired group consisted of 112 men who had been employed by a large manufacturing company in New Jersey, in jobs ranging from unskilled to supervisory and professional positions. About three years before the study was conducted, the company had instituted a new pension plan with a compulsory retirement clause which required workers to retire at 65 or at 60, in cases in which the worker was totally disabled. Data on retirement attitudes were furnished by a questionnaire mailed to 181 men, all those on retirement under the new pension plan. Replies were received from 112, representing a 62 per cent return. Since the respondents who returned the questionnaire may constitute a biased sample, caution should be exercised in the interpretation of the data.

The noncompulsory retired group, previously studied by Tuckman and Lorge, consisted of 216 men, a representative sample of retired, unionized, male industrial workers in the most highly skilled section of a major industry

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in New York City.[4] These workers were not required to retire at any specified age, but could retire at 65 if they wished to do so. Data on retirement attitudes were gathered by interviewing respondents at union locals or in their homes.

The two groups were quite similar in age, length of time in retirement, marital status, and living arrangements. For the compulsory retired group, the mean age at retirement was 68.5 years; for the noncompulsory retired group, 68.6 years. For the compulsory retired group, the mean length of time in retirement was 1.9 years; for the noncompulsory retired group, 2.8 years. Of the compulsory retired group, 71 per cent were married and 17 per cent widowed; of the noncompulsory, 79 per cent were married and 16 per cent widowed. Seventy-nine per cent of the compulsory retired group and 86 per cent of the noncompulsory were living in their own homes.

Attitudes Toward Retirement

Sixty-seven per cent of the compulsory retired group and 65 per cent of the noncompulsory retired group reported that they did not want to retire. It appears that there has been some shift toward greater acceptance of retirement after they had actually retired. For the compulsory group, 55 per cent reported that they liked retirement now, 43 per cent that they disliked it, and 2 per cent did not answer the question. For the compulsory group the responses were quite similar, with 50 per cent liking retirement and 50 per cent disliking it. However, written comments, such as "I have to like it" or "I have to accept it" made by some respondents, suggest that liking retirement may merely mean accepting the reality of the situation. Of those liking retirement, 42 per cent of the noncompulsory group and 11 per cent of the compulsory gave poor health or old age as reasons for their attitude. This suggests that their attitude is more indicative of their recognition that they are no longer able to work than of a positive acceptance of retirement. The shift toward acceptance is more apparent than real.

Fitness to Continue Working

Although there is no difference between the two groups with respect to attitudes toward retirement, the reasons for the attitudes, presented in the table, show important differences with respect to fitness to continue working. Twenty-nine per cent of the noncompulsory group, compared with 6 per cent of the compulsory, mentioned poor health or old age; 22 per cent of the noncompulsory, compared with 2 per cent of the compulsory, stated that they would prefer to work but could not do so because of illness. By contrast, 15 per cent of the compulsory group and none of the noncompulsory reported that they were able to work. The fact that only 13 per cent of the compulsory group referred to health in their feelings about retirement would seem to indicate that poor health was not a factor. There are no significant differences between the two groups with respect to the proportion who mentioned the following reasons: financial pressure, no way to pass the time, the desire to rest, to enjoy life, the feeling they had worked long enough, and other motives.

The difference between the two groups with respect to fitness to continue working is reflected in self-reports of some aspects of job performance prior to retirement, as shown in the table. Eighty-five per cent of the compulsory group compared with 33 per cent of the noncompulsory reported that, prior to retirement, they were able to turn out as good a day's work as they had five years before. Moreover, the compulsory group did not have to work as hard as the noncompulsory to turn out as good a day's work as they had previously. For the compulsory group, 23 per cent reported that they had to work harder compared with 81 per cent for the noncompulsory. Twenty-one per cent of the

compulsory group compared with 52 per cent of the noncompulsory reported that they turned down overtime work more frequently than they had five years prior to retirement. Of those who turned down overtime work more frequently, the majority stated they did this for health reasons. Twenty-five per cent of the compulsory group compared with 84 per cent of the noncompulsory reported that travel to and from the job was more tiring than it had been five years before retirement. Thirteen per cent of the compulsory group compared with 51 per cent of the noncompulsory reported that prior to retirement they were worried about not being able to keep up with younger workers.

Seventeen per cent of the compulsory group compared with 36 per cent of the noncompulsory reported that younger workers tease and annoy older workers. This suggests that the more adequate job performance of the compulsory group may result in a better relationship with younger workers within the plant than that among the noncompulsory group.

Plans for Retirement Period

The difference between the two groups with respect to reported fitness to continue working is reflected in plans for the retirement period. The activities planned are given in the table. For the noncompulsory group, 51 per cent planned to take it easy, compared with 22 per cent of the compulsory. For the noncompulsory group, 32 per cent had given no thought to what they were going to do, compared with 17 per cent of the compulsory. By contrast, 43 per cent of the compulsory group planned to find part- or full-time employment, compared with 5 per cent of the noncompulsory, who planned to find paid or volunteer work. A higher proportion of the compulsory group than of the noncompulsory—12 and 3 per cent—planned to take care of the house or sick wife. A higher proportion of the compulsory group than of

DATA ON RETIREMENT ATTITUDES

	Compulsory retirement group (n=112) %	*Noncompulsory retirement group (n=216)* %
*Reasons for attitude**		
Poor health, old age	6	29
Would rather work but not able	2	22
Still able to work	15	0
Desire to rest, to enjoy life, worked long enough	28	24
No way to pass the time	11	8
Financial pressure	9	7
Health better now	5	0
Other reasons	8	9
Not stated	16	0
Self-reported work performance prior to retirement		
Able to turn out as good a day's work as five years before	85†	33
Need to work harder to do so	23†	81
Turn down chance to work overtime more	21†	52
More tired in traveling to and from work	25†	84
Worried about not being able to keep up with younger workers	13†	51
Plans for retirement activity‡		
Paid or volunteer work	43†	5
Take it easy	22†	51
Educational activities	21†	5
Family care	12†	3
Visiting and recreation	9	7
Travel	9	3
Move to farm	4	0
Other	0	1
Hadn't thought about it	17†	32
Not stated	4	0
Actual retirement activities‡		
Housework or other work	64†	31
Sedentary—inside	24†	56
Sedentary—outside	0†	32
Nonsedentary	17	21
Educational	16	26
Social	8†	23
Religious	0	20
Family	0†	12
Travel	3	0
Other	4	1
Not stated	14†	0

*Two compulsory cases omitted; attitude not stated.
†Significant at .01 level.
‡Totals of percentage columns are greater than 100 because of multiple responses.

the noncompulsory—21 and 5 per cent—planned to engage in some educational activity such as pursuing a hobby, reading, or taking formal courses. There is no difference between the two groups with respect to the proportion who had planned to engage in recreation and visiting, travel, or other activities.

Retirement Activities

The way in which the respondents spend their day in retirement, as shown in the table, also indicates important differences between the two groups. Eighty-eight per cent of the noncompulsory group, compared with 24 per cent of the compulsory, reported that they engaged in sedentary inside and outside activities such as eating, sleeping, resting, taking it easy, sitting in front of the apartment house or in the garden, going to a movie or a ball game, watching television, listening to the radio, or doing just nothing. By contrast, 64 per cent of the compulsory group compared with 31 per cent of the noncompulsory engaged in some type of work activity. For the noncompulsory group this consisted almost entirely of housework, cooking, shopping, and, occasionally, such activities as babysitting, taking care of the grandchildren, and the occasional odd job. For the compulsory group, these activities were also included, but of those engaging in this type of activity, more than 25 per cent full- or part-time paid employment.

Twenty per cent of the noncompulsory and none of the compulsory reported attending church or synagogue. Twelve per cent of the noncompulsory group and none of the compulsory reported that they occupied themselves with their families—that is, visiting children, relatives, and talking about their grandchildren. Twenty-three per cent of the noncompulsory group, compared with 8 per cent of the compulsory, reported engaging in social activities, such as visiting friends, chatting with the neighbors, going to meetings, or attending a social club. There was no significant difference between the groups with respect to the percentage engaging in educational activities, travel, or nonsedentary activities.

The compulsory group's failure to mention activities concerned with religion and family, as well as their reporting less activity of a social nature, does not necessarily mean that these respondents did not participate in such activities. Rather, it may mean that these activities did not assume as much importance in day-to-day living for the compulsory group as for the noncompulsory because of preoccupation with work activity.

Conclusions

The findings of this study do not support the hypothesis that workers retired under a policy of compulsory retirement are more resistant to retirement than those retired under a policy of noncompulsory retirement. Although both groups are equally resistant, the reasons for their attitude differ a great deal. In the compulsory retired group, the resistance seems to stem from feelings about fitness to continue working, while in the noncompulsory retired group, the resistance stems from inability to continue working because of poor health or old age. In respect to fitness to continue working, the two groups show important differences about some aspects of job performance prior to retirement, plans for the retirement period, and ways for using leisure time in retirement.

The data utilized in this study were collected under contract of the Center for Improving Group Procedures, Teachers College, Columbia University, New York City.

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Editorial

Aging and drug reactions

FOR YEARS, pediatricians kept trying to find out wherein the body chemistry of children differed from that of adults, and, when there was a difference, they had to find out how great it was. They also had to learn the proper doses of drugs to be given to children and which drugs were likely to have special effects or bad side effects in children.

Now gerontologists are studying the unusual reactions of elderly patients to drugs and various types of therapy. In this issue of *Geriatrics* is to be found a most helpful paper by Doctors Moyer, Kinard, Conner, and Dennis, "Drug Therapy of Hypertension in the Elderly Patient." They studied the reactions of 541 average hypertensive patients to treatment with several drugs and compared these reactions to those of 97 similarly hypertensive patients over 60. The doctors studied also the incidence of side effects associated with the treatments in the two groups of the middle-aged and the elderly.

Actually, the responses to antihypertensive measures and drugs was about the same in the two groups of patients. With the less potent drugs such as Rauwolfia and hydralazine, the responses were slightly less noticeable among the older patients.

This study is of particular importance—partly because hypertension is so common in the aged and partly because a number of the drugs used in the treatment of hypertension have powerful effects on the autonomic nervous system. Also, because of the high incidence of small injuries of the brain caused by thromboses of small blood vessels or by oxygenation of the brain tissue, it is good to learn that forced reduction of blood pressure did not seem to carry any more danger in the aged patients than in those of average age.

Among the elderly patients, the systolic pressure dropped to normal in 24 per cent as compared with 33 per cent in the middle-aged group. This drop helped the elderly persons just as it helped the middle-aged.

WALTER C. ALVAREZ, M.D.

The first Pan American Congress on Gerontology

YOUR EDITOR has just returned from Mexico City, where he attended the first Pan American Congress on the many problems of aging. Some 800 men and women came from many countries to discuss such things as the relation of fats in the diet and the blood to atherosclerosis. Particularly manifest was the rapidly increasing interest of government bureaus, business heads, labor union leaders, hospital superintendents, owners of nursing homes, and many welfare workers in providing adequate care for the aged in general, and particularly for retired persons, for those

who are mentally or physically crippled, and for those who could still earn some money if they were helped to get a job or allowed to work.

There were papers by men who have been studying the body chemistry of aging animals and the histologic changes in aging tissues. Efforts are being made to find out why tissues and bodies age and die. There were papers on ways in which we physicians may some day be able to slow the processes of aging. Speakers discussed why some persons are old and worn out at 50, while others are spry, active, and keen at 80. What have heredity, diet, and hard work got to do with these changes? What has gone wrong in a man's brain when, before his time, he gets crabbed and "sot in his ways," or unable to work?

Mr. Robert Peterson noted the interesting fact that newspaper editors have recently discovered that now, with so many oldsters in every community—and their number constantly increasing—anything on diseases of the aged and on problems of retirement is news, and well worth publishing for it will interest many readers.

Interesting was Dr. Reuben Kahn's description of Emeritus Hall at Palm Beach—an endowed institution to which any retired, but still active professor can go with his wife to live comfortably while they finish a bit of research or write a book. How much good such an institute can do!

Great credit must go to Dr. Payno, Dr. Cowdry, and others on the organizing committee who planned the Congress, and carried out the enormous correspondence necessary to bring to Mexico City the hundreds of delegates from all over the world. Just the publishing of the good-sized book of abstracts of the papers, with a translation of each abstract, was a tremendous job.

It must have taken an enormous amount of time and work to plan all of the many entertainments for the members of the Congress! Commendable was the skill of the translator who rapidly changed English into Spanish or Spanish into English, as the speaker was giving his paper.

It was unfortunate that there was no one hotel large enough to take most of the delegates and to supply a hall for the talks. The meetings had to be held at the University, which is far out from the center of the City of Mexico, and not supplied with taxi service. Because of the scattering of the delegates there was little opportunity for discussions and for the making of the friendships that are so desirable at a Congress.

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Publicity and public fascination with the very old

THE AMERICAN PUBLIC, long bombarded with cultivated excitement over the tallest skyscrapers, colossal movie films, theatrical extravaganzas, built-up glamor in women, furs, and automobiles, the more recent TV spectaculars and modern advertising methods of publicizing the new by spreading superlatives more thickly than any growing boy spreads jam on fresh bread, is assumed to be fascinated only by the unusual, the bizarre, or the "biggest" yet. How much of the assumption is valid we do not know, but that it is valid in part is indisputable. Editors and advertisers clearly find such publicity profitable. We are obviously proud of our biggest aircraft carrier—too big for the locks of the Panama Canal and so large it becomes a target more vulnerable than two or three smaller but dispersed vessels—and want to have the biggest planes, corporations, bridges, and waistlines. Bigness is assumed to parallel greatness. Notori-

ety is given maximal value. Consequently, real and lasting worth is often unseen.

Thus it is that anything or anyone to which ultimate superlatives can be applied becomes news. Two recent examples of attainment to this criterion are "the last of the Boys in Blue," Albert Woolson, of Duluth who died aged 109, and the Colombian Indian, Javier Pereira, who claims to be 167, the "oldest man in the world." The furor in the press over these two examples of extreme longevity, one can be sure, stems not from any significant advancement of scientific knowledge, but from the habit of pushing publicity of the peculiar or maximal.

Javier Pereira is still alive and was available for clinical study. According to the press, a most thorough evaluation of his physical condition was made at the New York Hospital-Cornell University Medical Center. How extensive this was, except for thorough x-ray examination, we will not know until the scientific report is published. The data given to the press have been so inflated by optimistic unrealistic dramatization that the popular reports are essentially worthless. There has been revealed no proof that this man is more than 110 or perhaps 120 years old; the medical examiners are quoted as saying "he *may be* as old as 150." "May be" means it is *possible*, which is quite different from *probable*. To some I "may be" a truly nice man; it is far more probable that I am merely an acidulous and unrepentant iconoclast.

Geriatric medicine is interested in the very old, and in learning what changes age *per se*, in the absence of disease, produces in the body structures and functions. That is why we await the scientific reports from New York with considerable interest, and are intensely curious anent the scope and nature of the clinical and physiologic studies undertaken. Were they all focused upon the discovery and identification of disease? Or was an effort made to evaluate the old man's health? The two approaches are not synonymous (Stieglitz, E. J.: Geriatrics 10: 151, 1955 and Medical Annals of the District of Columbia 25: 207, 1956). Health is far more than the absence of disease; it involves the reserve capacities of all the functional activities of the organism. Such reserves are revealed only under conditions of stress. Were stress tests conducted in this clinical evaluation? We do not yet know; we only can hope so. Clinically applicable methods for the mensuration of health are sadly lacking, and the dearth of studies directed toward such an end is even more unfortunate. Medical science has been so preoccupied with disease that it has blindly and unwisely neglected the study of health in general and in relation to age in particular.

"Drummer Boy" Albert Woolson contributed almost nothing to advancing scientific knowledge anent advanced age. So far as present public knowledge goes, there was no postmortem examination. If this is correct, it is unfortunate but typical. Are physicians and pathologists *really* interested in studying tissues of those who pass the century mark? It is to be doubted. In 1945 there was established a Registry for Gerontology in the Army Medical Museum in order to collect tissues, specimens, and slides from the very old, just as the other registries assemble, file, and index thousands of specimens of various tumors, retinal lesions, and so on. But in the eleven years since the Registry for Gerontology was created not one case and not one bit of material has been submitted!

The truly scientific significance of those instances of exceptional longevity, in contrast to the "popular fascination" with the bizarre, is limited to a few rather general and tentative interpretive impressions.

First, they should serve to remind us of the medical profession that only a very, very few individuals die or are disabled by old age *per se*. Almost all die of disease.

Second, the very rarity of these people makes study of the reasons why they were able to escape or avoid disease especially difficult. In some instances, as with the Colombian Indian, Javier Pereira, it has been possible to elicit information regarding lifelong dietary habits, but knowledge concerning hereditary background is usually unavailable. Yet we know that the inherited endowment has much to do with life expectancy.

Third, despite the numerical scantiness of collected observations, it is apparent that most, if not all, of those surviving over a century are of small stature and lean. The obese do not live so long. The smallness of stature, as in Pereira, who is reported to be but 52 inches tall and to weigh only 75 pounds, coincides and confirms in human beings McCay's classical prolongation of the life span of rats by retarding or stunting their growth with balanced but calorically restricted diets. Whether the fact that 85 per cent of Pereira's diet has been carbohydrates is significant or not we do not know. Clearly it has not been fully an adequate diet as evidenced by his severe anemia (hemoglobin, 7 gm. or 44 per cent, and red blood cell count 2,500,000).

Fourth, so far as my fallible memory serves, the great majority of known centenarians are, and have been, decidedly simple folk. Simple in mind, direct, incurious, and with readily satisfied ambitions. Simple in modus vivendi; essentially noncompetitive, resident in a peaceful environment which is usually rural and often nearly primitive. They have lived relatively isolated from massed humanity and thus perhaps avoided both bacterial and psychologic contagion. They do not become involved in the stresses and conflicts which are induced when men are concentrated in civilized cities. There is more than the suggestion that the majority are or have been what aggressive, vigorous, competitive, and approval seeking moderns would call "lazy." It is questionable whether this is true laziness or indolence; perhaps it is innate wisdom. They know what they want and, as the wants are simple, they are fulfilled without undue striving. They are not stupid folk, for simple and stupid are not the same. But in their simplicity they stick to fundamentals and are not led astray by slogans, fatuous promises, and dreams of greatness.

Most "oldest inhabitants," when interviewed by the press on their ninetieth, ninety-fifth, or hundredth birthday are delighted to reveal their own pet formula to explain their unusual longevity. Perhaps they really believe these formulae; perhaps they are created to make copy and please the reporters. They reveal nearly as many contradictions as there are centenarians: plenty of liquor versus total abstinence, heavy use of tobacco versus abhorrence of the filthy weed, fresh air versus a shut-in life, and so on. One old gentleman attributes his great age to his having carefully cultivated the habit of breathing, and another to delight in wine, women, and song until his physician forced him to give up singing. But perhaps the best formula was that offered by a bright and chipper Mammy of 104 who said: "When I worked, I worked hard; when I set, I set loose; and when I began to worry, I went to sleep." Would that more of us could learn to do that!

Maximal length does not necessarily give maximal depth and breadth in life. When all three dimensions are significantly large, then and only then, can one speak of "*great* age."

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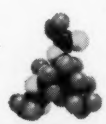

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Digests FROM CURRENT LITERATURE

Hip Operations in the Elderly

O. J. VAUGHAN-JACKSON. Med. Press. 236: 241-246, 1956.

Hip surgery in elderly patients is indicated in degenerative arthritis when there is persistent, disabling, and unrelieved pain, and in fracture of the upper end of the femur. The painful joint may be made insensitive by division of the obturator nerve and the nerve to the quadratus femoris. Pain may be relieved by capsulectomy, which interferes little with the femoral head and subjects the patient to little surgical trauma, but gives unreliable results.

The ideal solution is to fashion a workable joint. In the mold arthroplasty of Smith-Petersen, the surfaces of the femoral head and acetabulum are removed, and a smooth vitallium cup-shaped mold is interposed. The long period of nonweight-bearing and remobilization exercises make careful selection of patients essential. Complications are impairment of the vascular supply of the femoral head and neck, or displacement or incarceration of the cup.

In the Judet arthroplasty replacement procedure, a large portion of the femoral head is removed, and a mushroom-headed prosthesis with an intramedullary peg is inserted into the femoral neck. Results are satisfactory for about three years. In patients with a short life expectancy, this is the method of choice.

Among methods without prostheses is the Gathorne-Girdlestone procedure in which an excision is made through the base of the femoral neck. The femoral shaft rides up, causing the patient to walk with a pronounced Trendelenburg limp. The Batchelor excision of head and neck of the femur combined with a subtrochanteric osteotomy gives very satisfactory results, and is suitable for elderly patients.

Another approach is to alter the hip joint by either the McMurray osteotomy or the Charnley central displacement arthrodesis. The advantage of osteotomy is the tendency for hip function to improve rather than to deteriorate with time.

Pinning of a fractured femoral neck with a Smith-Petersen trifin nail should be used only when it is possible to prevent weight-bearing until bony union has occurred. Simple procedures with short periods of convalescence are desirable in the extremely elderly.

(Continued on page 44A)

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ADMINISTRATION. Although Shalowitz found the optimal dose was 10 mg. tablets three or four times a day, some patients may respond better on the 25 mg. tablets, b.i.d. or t.i.d. Now also available in syrup form, containing 10 mg. ATARAX per tsp. In tiny 10 mg. (orange) and 25 mg. (green) tablets, bottles of 100. ATARAX Syrup in pint bottles.

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1. Shalowitz, M.: Hydroxyzine: a new therapeutic agent for senile anxiety states. Geriatrics 11:312 (July) 1956.

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Digests FROM CURRENT LITERATURE

(Continued from page 42A)

Environmental Change and Age of Onset of Psychosis in Elderly Patients

C. BUCK, J. M. WANKLIN, and G. E. HOBBS. Arch. Neurol. & Psychiat. 75: 619-623, 1956.

Environmental changes of an uprooting or isolating nature appear to accelerate onset of psychotic behavior in susceptible elderly individuals. In a study of 516 mental hospital patients 65 and over, the expected age of onset of psychosis was determined by statistical analysis. The average age at onset of the whole group was compared with the actual age at onset of 245 patients who experienced an environmental change before mental disability appeared. Only patients subjected to a change after age 40 were included in the study.

Men who had retired and had moved to a geographic area of different population size had mental disorders 2.9 mean years earlier than was statistically expected. Retirement alone did not accelerate time of onset of psychosis. Among women with a combined change of residence and home situation—living with children or relatives as a result of widowhood—mental disorders occurred 3.1 mean years earlier than expected. In both sexes, two environmental changes occurring together accelerated time of onset.

Evaluation and Preparation of the Patient with Degenerative Cardiovascular Disease for Major Surgery

J. S. LA DUE. Bull. New York Acad. Med 32: 418-434, 1956.

Degenerative cardiovascular disease occurs in 70 per cent of patients over 70 and is the leading cause or contributory cause of death following major surgery in the aged. The mistake of attempting to explain vague complaints as a natural aging process often leads to late recognition of significant abnormalities. Devoted care, with special attention to detail, is especially needed in the care of the elderly surgical patient. Improvements in anesthetic technics; prompt and intelligent use of antibiotics; exact information regarding blood volume, electrolyte imbalance, and nutritional needs; and, of vital importance, immediate recognition and treatment of postoperative complications will do much to make major operations relatively safe in the aged.

Operative risk can be estimated with greatest accuracy if an estimate of the patient's physiologic age is used rather than actual chronologic age. Bundle-branch block, healed myocardial infarction, or auricular fibrillation do not appreciably increase operative risk. The most serious cardiovascular complications after surgery are acute myocardial infarction and uncontrollable arrhythmias.

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Dosage: *Geriatric Patients*—1 mg. Meratran once or twice daily. Observe patient response, adjust dosage to individual needs.

Contraindications: Meratran is contraindicated in agitated prepsychotic patients, paranoia or in certain other cases such as obsessive-compulsive states.

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References: 1. Pomeranze, J.: J. Gerontol. 9:486, 1954. 2. Kleemeier, R. W.; Rich, T. A., and Justisz, W. A.: J. Gerontol. 11:165, 1956. 3. Brown, B. B., and Werner, H. W.: Federation Proc. 12:304, 1953. 4. Brown, B. B., and Werner, H. W.: J. Pharmacol. & Exper. Therap. 110:180, 1954. 5. Biohm, T. R., et al.: Federation Proc. 13:237, 1954. 6. Anton, R. J.: Arizona Med. 11:397, 1954.

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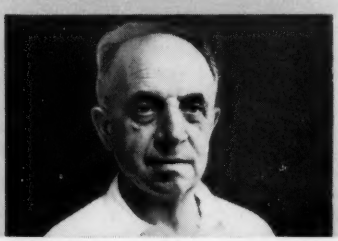
alertness seen on second day of 1.0 mg. Meratran—resumed old interest in Mission work in 3 weeks—"great improvement . . . has gotten along extremely well."



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Book Reviews

Mental Disorders in Later Life

O. J. KAPLAN, Editor, 1955. Second edition, Stanford, California: Stanford University Press. 508 pages. $7.50.

This is the second edition of a volume of papers first published in 1945. The editor's comment that the "field of gerontology has experienced tremendous growth" in the ensuing ten years speaks more of enthusiasm than careful appraisal in view of the fact that the new volume contains only two new chapters and the editor's note that some of the chapters "are as up to date today as when they were written." The relative stability of this book's content is not a serious criticism of it; in its first edition it was a sound and useful compendium of facts and concepts concerning mental disorders of the presenium and senium, and it remains so.

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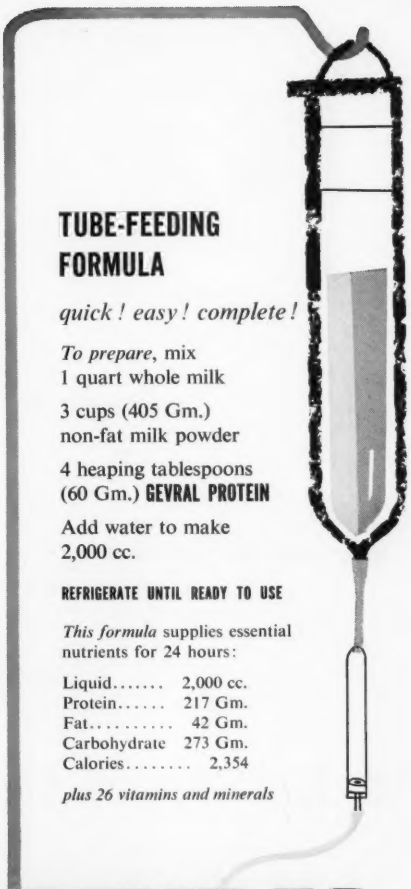
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Book Reviews

(Continued on page 47A)

The editor chose his contributors with considerable care. With few exceptions they are authorities in the fields of medicine, psychology, and sociology, who are readily recognized for persistent interest and research into the problems of the aged. Included are chapters by Nathan Shock, Harold E. Jones, H. Warren Dunham, Norman Cameron, Eugene Davidoff, David Rothschild, and Nolan D. C. Lewis.

The two new chapters in this edition cover widely separate topics: Franz Kallman's "genetic aspects" and the use of electric shock therapy by Prout, Allen, and Hamilton. Kallman's chapter is heavily packed with intriguing data. For example, he relates that on three out of four pairs of senescent one-egg twins, deaths of highly similar cerebrovascular complications occurred in both twins within one month, despite considerable differences in life histories. He concludes, "further advancement in the understanding of involutional, arteriosclerotic, and senile psychoses will require the planning of more basic research in relation to the interplay of such complex determinative components as age-susceptible personality traits, reduced adaptive homeostatic plasticity, and those genespecific biochemical phenomena controlling growth and decline."

The chapter by Clive McCay on "Food for the Later Years" is a highly practical digest of factual information and source materials on the nutritional needs, digestive problems, and dietary titillation of the aged. It is generally true of the chapters in this volume that they are closely reasoned, factually detailed, and generally free of the froth and foam which sometimes characterize collections by experts who appear to have contributed to a "symposium" in the original sense, rather than to have furnished food for thought. Actually, these chapters have so much material that they would all have an increased usefulness if they had ended with the pointed, report-like summary which is found in less than half of them. Fortunately, such summaries are found in those chapters having greatest need of them.

This book by no means replaces or outdates the first edition. However, it is a valuable and well-edited reference work containing information and suggestions which will be found useful by physician, psychiatrist. and psychologist. Those who do not have the first edition will find that this one makes a worthy addition to their professional library.

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Minneapolis, Minn.

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Activities and Announcements . . .

Coming Meetings

The *National Committee on the Aging* of the National Social Welfare Assembly will hold its annual meeting at the Barbizon-Plaza Hotel, New York City, December 12 and 13, 1956, and the spring meeting at Whittier Hotel, Detroit, Michigan, on April 4 to 6, 1957. Theme for the spring meeting will be "Maintaining Independence in Old Age." For further information write the National Social Welfare Assembly at 345 East 46th Street, New York 17.

The *New York Heart Association* is planning a one-day conference on "Atherosclerosis and Coronary Heart Disease" to be held at the Waldorf-Astoria Tuesday, January 15, 1957. Dr. Robert L. Levy is chairman of the steering committee. Speakers will include Dr. Paul D. White, Dr. E. Cowles Andrus, Dr. Herman E. Hilleboe, and Dr. Ancel Keys.

The Fourth Congress of the *International Association of Gerontology* will be held in Merano, Italy, July 14 to 19, 1957. For registration forms and further information, write to the secretary, Quarto Congresso Internazionale de Gerontologia, Viale Morgagni, 85, Firenze, Italy.

Third Merrell Symposium on Aging

The third annual Merrell Symposium on Constructive Medicine in Aging will be held at the Netherland Hilton Hotel in Cincinnati on January 17, 1957. The subject for the 1957 meeting, which is open to all interested physicians, will be *Cardiovascular Disorders in the Aging*. Papers will be presented by the following speakers:

K. J. Franklin, Medical College of St. Bartholomew's Hospital, London, "Investigation of What Is Considered Normal for the Aging Cardiovascular System"

J. Earl Estes, Jr., Mayo Clinic, Rochester, Minnesota, "Venous Disorders in Older People"

Walter S. Priest, associate professor of medicine, Northwestern University School of Medicine, "Anticipation and Management of Cardiac Decompensation"

Jessie Marmorston, professor of experimental medicine, University of Southern California, "Hormonal Aspects of Myocardial Infarction in Female and Male Subjects"

Ancel Keys, professor of physiology and director of the Laboratory of Physiological

(Continued on page 53A)

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for safe, effective treatment of moderately disturbed aged patients...

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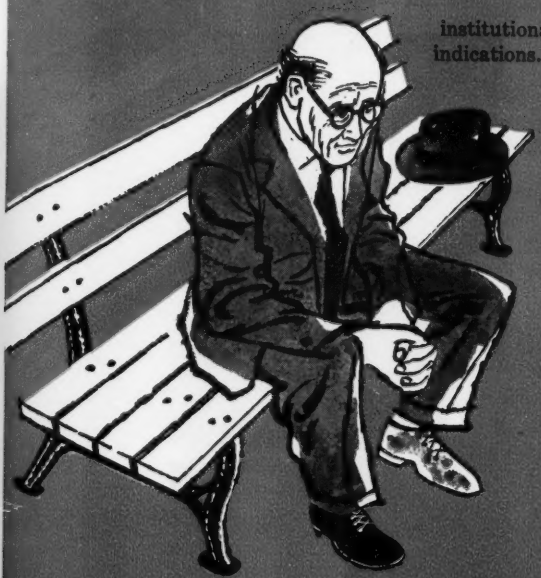

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Activities and Announcements . . .

(Continued from page 50A)

Hygiene, University of Minnesota, "Calories and Cholesterol"

Robert W. Wilkins, associate professor of medicine, Boston University School of Medicine, "Drug Therapy for Hypertensive Vascular Disease in Patients Past Midlife"

Robert A. Bruce, associate professor of medicine, University of Washington School of Medicine, "Evaluation of Functional Capacity in Patients with Cardiovascular Disease"

Edward J. Stieglitz, consultant in geriatrics, Veterans Administration and St. Elizabeth's Hospital, Washington, D. C., "Integrated Unity of the Patient"

•

Center for Aging Research

The National Institutes of Health, Bethesda, Maryland, have established a Center for Aging Research as part of the Public Health Service's program to coordinate and accelerate all of its activities in the field of aging.

EDITOR'S NOTE

In the article, *Management of Dupuytren's Contracture*, by Lee J. Cordrey, M.D., which appeared on page 441 of the October issue of Geriatrics, *Dupruyten's contracture* should read *Dupuytren's contracture.*

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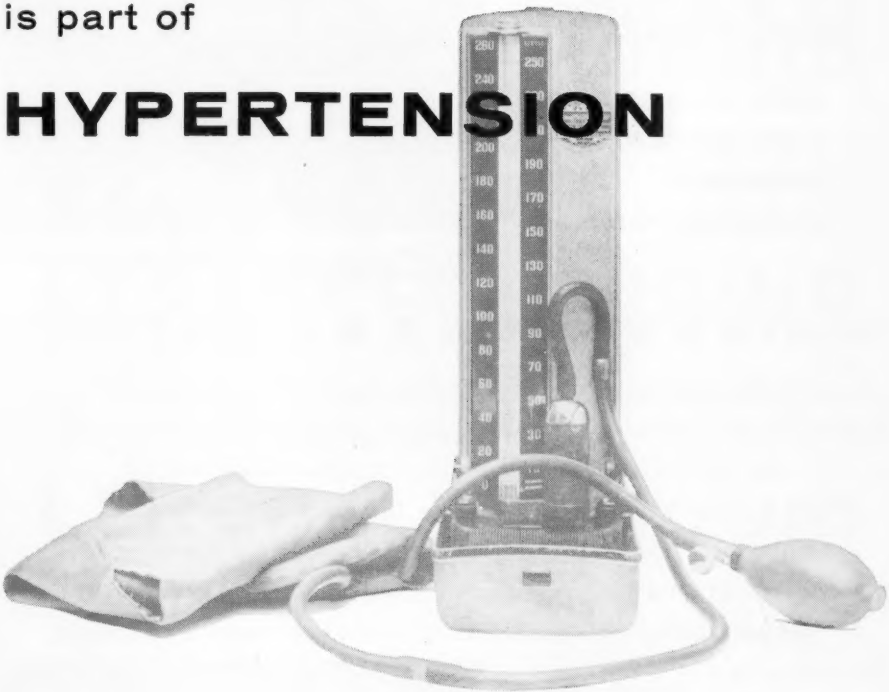

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℞ in 1½ oz. or 4 oz. tubes;
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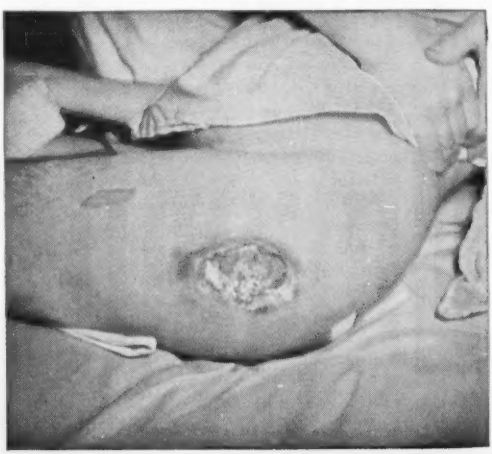

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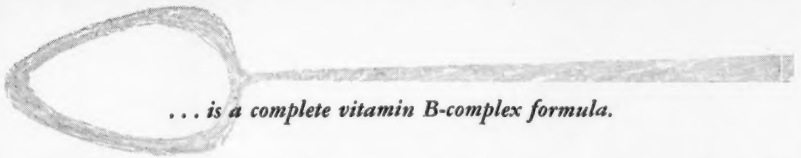

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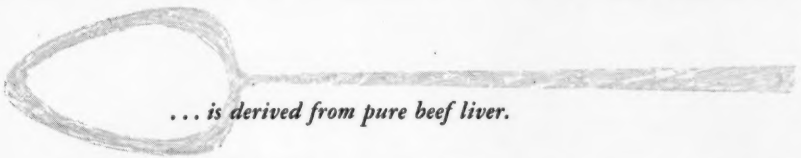

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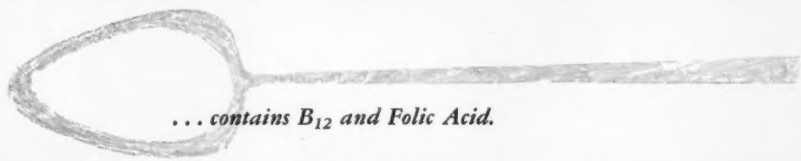

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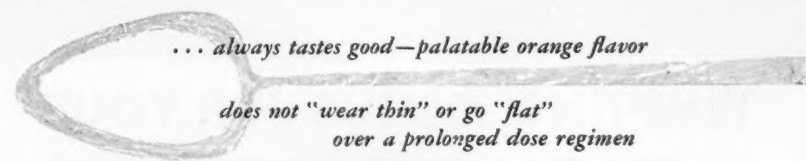

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[1]Levy, S.: J.A.M.A., 153:1260-1265, 1953.

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(1) Griffith, J. Q., Jr.; Naghski, J., and Krewson, C. F.: Rutin and Related Flavonoids, Easton, Pa., Mack Publishing Co., 1955. (2) Griffith, J. Q., Jr.: M. Clin. North America 38:1717, 1954.

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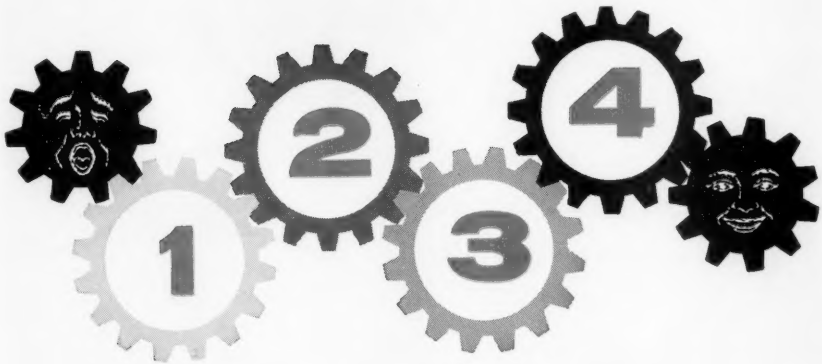
and calm the patient



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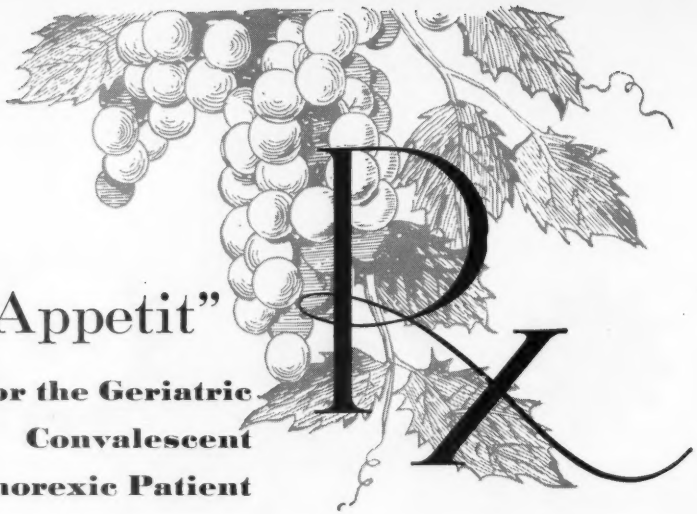

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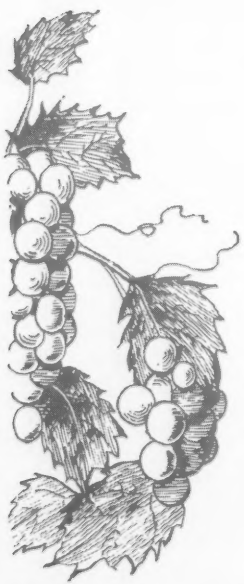

- wine stimulates olfactory acuity—markedly increasing appetite in anorexia
- wine serves as a quick-energy food. Its small amount of hexose is speedily absorbed and its moderate content of alcohol is metabolized readily even by diabetics
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—Glass, G. B. J.: Personal communication, 1956.

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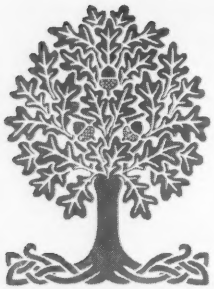

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PROGRAM

Johnson McGuire, Professor of Clinical Medicine and Director of Cardiac Laboratory, University of Cincinnati College of Medicine, will serve as moderator for the Symposium

K. J. Franklin, The Medical College of St. Bartholomews Hospital, London.
INVESTIGATION OF WHAT IS CONSIDERED NORMAL FOR THE AGING CARDIOVASCULAR SYSTEM

J. Earle Estes, Jr., Mayo Clinic, Rochester, Minnesota.
VENOUS DISORDERS IN OLDER PEOPLE

Walter S. Priest, Associate Professor of Medicine, Northwestern University School of Medicine, Chicago.
ANTICIPATION AND MANAGEMENT OF CARDIAC DECOMPENSATION

Jessie Marmorston, Professor of Experimental Medicine, University of Southern California, Los Angeles.
HORMONAL ASPECTS OF MYOCARDIAL INFARCTION IN FEMALE AND MALE SUBJECTS

Ancel Keys, Professor of Physiology and Director of Laboratory of Physiological Hygiene, University of Minnesota, Minneapolis.
CALORIES AND CHOLESTEROL

Robert W. Wilkins, Professor of Medicine, Boston University School of Medicine, Boston.
DRUG THERAPY FOR HYPERTENSIVE VASCULAR DISEASE IN PATIENTS PAST MIDLIFE

Robert A. Bruce, Associate Professor of Medicine, University of Washington School of Medicine, Seattle.
EVALUATION OF FUNCTIONAL CAPACITY IN PATIENTS WITH CARDIOVASCULAR DISEASE

Edward J. Stieglitz, Consultant in Geriatrics, Veterans Administration and St. Elizabeths Hospital, Washington, D. C.
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References

1. Stare, F. J.: *Bull. New York Acad. Med.* **32**:284, 1956
2. Kaufman, W.: *J. Am. Geriatrics Soc.* **3**:927, 1955
3. Kinsell, L. W.: *J. Am. Geriatrics Soc.* **3**:31, 1955
4. Kaplan, L.; Landes, J. H. & Pincus, J.: *Geriatrics* **10**:287, 1955

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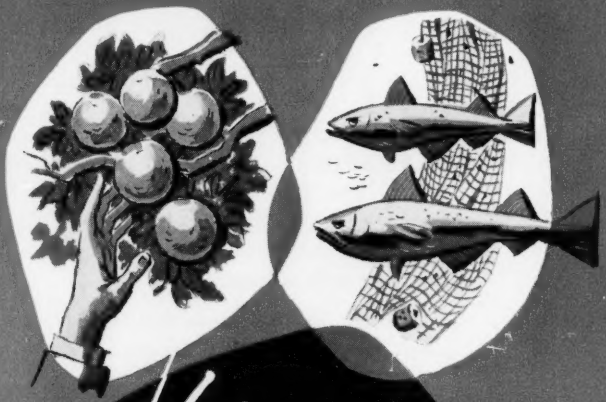

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1. Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared—Washington, D.C., United States Department of Agriculture, Agricultural Handbook No. 8, 1950.

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In the problems of geriatric nutrition, of dealing with the self-imposed restrictions and distorted appetites of the aged, oatmeal offers definite advantages. It provides good protein, valuable vitamins and minerals, is low in sodium and purines, is easily eaten, readily digested, and promptly utilized.

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[1]Fuller, H. L. and Kassel, L. E.: Antibiotic Med. and Clin. Therapy, 3: 322, Oct. 1956.

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Bonica, J.J.; and Backup, P.H. (Tacoma General Hospital, Washington): *Northwest Med.*, 54:22, Jan., 1955.

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*Reifenstein, E. C., Jr., in Harrison, T. R.: Principles of Internal Medicine, ed. 2, New York, The Blakiston Company, Inc., 1954, chap. 98, pp. 702, 703.

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